Millimeter Waves

CURRENT STATE AND IMPLICATIONS OF RESEARCH ON BIOLOGICAL EFFECTS OF MILLIMETER WAVES: A REVIEW OF LITERATURE

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Running title: **"Bioeffects of Millimeter Waves"**

ABSTRACT

In recent years, research into biological and medical effects of millimeter waves (MMW) has expanded greatly. The present paper analyzes general trends in this area and briefly reviews most significant publications, proceeding from cell-free systems, dosimetry and spectroscopy issues, through cultured cells and isolated organs to animals and humans. The studies reviewed demonstrated effects of low-intensity MMW (10 mW/cm2 and less) on cell growth and proliferation, activity of enzymes, state of cell genetic apparatus, function of excitable membranes, peripheral receptors, and other biological systems. In animals and humans, local MMW exposure stimulated tissue repair and regeneration, alleviated stress reactions, and facilitated recovery in a wide range of diseases (MMW therapy). Many of reported MMW effects could not be readily explained by temperature changes during irradiation. This paper outlines some problems and uncertainties in the MMW research area, identifies tasks for future studies, and discusses possible implications for development of exposure safety criteria and guidelines.

Key words: **Electromagnetic fields, bioeffects, mm-wave band**

INTRODUCTION

The term "millimeter waves" (MMW) refers to extremely high-frequency (30-300 GHz) electromagnetic oscillations. Coherent oscillations of this range are virtually absent from the natural electromagnetic environment, which might have had important consequences. First, living organisms could not have developed adaptation to MMW during the course of evolution on Earth. Second, some specific features of MMW radiation and the absence of external "noise" might have made this band convenient for communications within and

between living cells [Golant, 1989; Betzky, 1992]. These arguments, though not adequately proven, are often used to explain high MMW sensitivity of biological subjects. Indeed, MMW have been reported to produce a variety of bioeffects, many of which are quite unexpected from a radiation penetrating less than 1 mm into biological tissues. A number of theoretical models have been set forth to explain peculiarities and primary mechanisms of MMW biological action [Fröhlich 1980, 1988 (ed); Golant, 1989; Grundler and Kaiser, 1992; Belyaev et al., 1993a; Kaiser, 1995].

One of the most remarkable events in contemporary electromagnetic biology is a surge in interest in MMW biological and medical effects in the countries of the former Soviet Union (FSU). A striking difference in the FSU and "non-FSU" research activity in this area can be seen from counts of related publications. For example, the EMF Database[1] v. 3.0 (1997) lists a total of 463 FSU publications on MMW-related topics, and only 261 such publications from the rest of the world. Though these numbers should not be taken as exact (the Database includes most, but certainly not all relevant citations), the situation in general is portrayed correctly and is particularly explicit in a historic perspective (Fig. 1). The non-FSU production reached its peak of 52 papers (including meeting abstracts) in 1983-1984, which was 3.3% of all non-FSU publications in the bioelectromagnetics area; then it gradually declined to only seven papers (0.5%) in 1989-1990. Concurrently, MMW research in the FSU expanded greatly: Both the count of publications (up to 120 in 1995-1996) and their portion in the FSU bioelectromagnetic research (20 to 30%) far exceeded these numbers for non-FSU publications.

Aside from the number of studies, there are important qualitative differences. Western (non-FSU) research was largely driven by concerns for public safety. However, safety issues occupy a relatively small portion of the FSU research, while far more studies are related to medical applications of MMW. Over 50 diseases and conditions have been claimed to be successfully treated with MMW alone or in combination with other means. Lebedeva and Betskii [1995] have reported more than a thousand MMW therapy centers in the FSU and over 3 million people received this therapy. Naturally, the extensive medical use of MMW has stimulated basic research as well.

Nowadays, MMW technologies are increasingly being employed in practical applications (e.g., wireless communication, traffic and military radar systems), making it imperative that bioeffects data be available for health hazard evaluation and restoring the interest to MMW biological research in the West. The number of non-FSU publications on this topic is again increasing, a specialized MMW session appeared at the 1996 and 1997 meetings of the Bioelectromagnetics Society, and the first Infrared Lasers and MMW Workshop was held at Brooks AFB, TX in 1997. Unfortunately, the FSU research, a rich source of MMW bioeffects data, is not readily available in the West and is scarcely known by Western scientists.

The present paper is intended to fill in this gap by looking over recent research in the MMW field, from molecules and cells to MMW therapy. We have analyzed over 300 original FSU publications and about 50 non-FSU papers, and selected those which appeared more interesting and credible. This review is primarily focused on experimental and clinical findings reported during the last decade; therefore, it includes only a few essential citations of earlier publications and does not cover such topics as theoretical modeling of possible interaction mechanisms. Interested readers should see other reviews for additional information [Fröchlich, 1980; 1988 (ed.); Gandhi, 1983; Grundler, 1983; Postow and Swicord, 1986; Belyaev, 1992].

1. PHYSICO-CHEMICAL EFFECTS, MMW ABSORPTION AND SPECTROSCOPY

A number of independent studies have shown specific MMW effects in the absence of living subjects, i.e., in solutions of biomolecules and even in pure water.

Fesenko and Gluvstein [1995] analyzed MMW effects on periodic voltage oscillations during a discharge of a water capacitor. The capacitor, which was a distilled water sample in a 1-mm capillary, was charged by 18 V, 1-ms wide unipolar rectangular pulses. The capacitor discharged within 500-600 ms after a pulse. The discharge curve contained periodic voltage oscillations reaching 10-15 mV. Fourier spectrum of these oscillations consisted of two strong peaks, at 5.25 and 46.8 Hz, and these peaks did not change during at least two hours of experimentation. The water sample was exposed at 36 GHz from an open-ended waveguide (7.2 x 3.4 mm cross-section). Irradiation at 50 m W output power greatly reduced the 46.8 Hz peak in 1 min and virtually eliminated it in 10 min, and also shifted the 5.25 Hz peak to 6.75 Hz. These changes showed little or no recovery within 20-60 min after cessation of a 10-min exposure. Irradiation at 5 mW output power produced similar changes, but, unexpectedly, was far less effective: the changes developed more slowly, and the original peaks restored more quickly. Mechanisms of the phenomenon itself, its anomalous power sensitivity, and the long-lasting "memory" of water were not understood. The authors suggested that MMW-induced changes in water properties could underlie biological effects.

Direct MMW effects on pure water properties were also observed by holographic interferometry [Berezhinskii et al., 1993; Litvinov et al., 1994]. Refraction of light in fluid was determined from the width and number of interference bands formed by a He-Ne laser beam (630 nm) passing through the fluid and a referent beam. Irradiation of distilled water at 10 mW output power for 5-7 min caused no effect at 41.5 GHz, but decreased the number of the interference bands from 6 to 5 at 51.5 GHz; the distance between the bands increased 1.2 times. These changes developed faster and were more profound in a 2% human blood plasma solution. The effect reached saturation in 6-7 min and was completely reversible. Both theoretical calculations and direct measurements established that maximum MMW heating was about 1 ^{o}C. MMW-induced changes in the light refraction coefficient were almost an order of magnitude greater than produced by 1 ^{o}C conventional heating, and therefore were attributed to a specific effect of MMW.

Other properties of blood plasma, such as dielectric permittivity and absorption coefficient, could be altered by MMW irradiation as well [Belyakov et al., 1989]. Changes in these parameters measured only 0.05-0.5%, but were well beyond the accuracy of the method used (0.01%). The sensitivity of plasma samples to particular radiation wavelengths strongly varied from one blood donor to another.

Khizhnyak and Ziskin [1996] analyzed peculiarities of MMW heating and convection phenomena in water solutions. Besides the most expected reaction (gradual temperature rise), irradiation could induce either temperature oscillations and a decrease in average temperature, or a biphasic response in which the temperature initially rises and then decreases. These anomalous effects resulted from convective processes, i.e., the formation of a toroidal vortex. When the vortex became stable, the temperature decreased following the initial rise phase, although the irradiation was constantly maintained. The local temperature could decrease with increasing power density, and in biological systems this would appear as an effect opposite to heating. Probably, this phenomena could explain some of reported "nonthermal" MMW effects. If irradiation continued for a long time (30-40 min), the convection phenomena disappeared and could not be reintroduced even after restoration of the initial temperature. This observation suggested that some irreversible

process had occurred in the liquid, which resembles findings of the water "memory" cited above.

The supposed role of water as a primary target for MMW radiation motivated Zavizion et al. [1994] and Kudryashova et al. [1995] to study how MMW absorption at the wavelengths of 2.0, 5.84, and 7.12 mm is affected by the presence of other substances, namely a -amino acids (0.25-2.5 mol/l). Since MMW absorption by amino acid molecules is negligible, the absorption of solutions, in most cases, decreased proportionally to the amino acid concentration. This difference in absorption by pure water and solutions, or "absorption deficit", increased with increasing the length of the hydrophobic radical in a series of homologous amino acids (glycine -alanine -GABA -valine). Paradoxically, the absorption deficit was negative for sarcosine at 5.84 mm and 7.12 mm, and for glycine at all the wavelengths, meaning that these two amino acids can increase MMW absorption by water molecules.

A detailed theoretical analysis of MMW absorption in flat structures with high water content was performed by Ryakovskaya and Shtemler [1983]. The authors produced dependencies of the specific absorption rate (SAR) on the radiation frequency, temperature, thickness of the absorptive medium, and presence of dielectric layer(s) above and/or underneath. This work modeled most common biological setups, such as irradiation of cell suspensions in Petri dishes, cuvettes, etc. The wavelength in the medium, reflection coefficients, depth of penetration, and SAR at the surface of a semi-infinite absorptive medium were calculated for wavelengths from 1 to 10 mm, with 1-mm steps. For example, the depth of penetration for 1- and 10-mm wavelengths at 20 °C equals 0.195 mm and 0.56 mm, respectively, and the surface SAR reaches 79.4 and 15.5 mW/cm3 per 1 mW/cm2. Exposure through a thin dielectric layer (e.g., bottom of a Petri dish) may decrease reflection and further increase SAR by up to 2.5 times. SAR in thin absorptive films (0.1-0.01 mm) increases greatly and may exceed SAR at the surface of a semi-infinite medium more than tenfold. Furthermore, presence of a dielectric above or below the thin absorptive film may increase SAR in it as much as 20-fold. Apparently, the possibility of reaching very high SAR levels and of local heating cannot be underestimated even for the incident power levels that are often regarded as nonthermal (0.1-1 mW/cm2).

2. MMW EFFECTS AT SUBCELLULAR, CELLULAR, AND TISSUE LEVELS

2.1 Growth rate effects

Debates about resonance growth rate effects of MMW have been going on for over 20 years, and this problem was widely discussed in earlier reviews. In brief, Grundler and co-authors [1977, 1982, 1988] reported that the yeast *Saccharomyces cerevisiae* growth rate may be either increased by up to 15%, or decreased by up to 29%, by certain frequencies of MMW within a 41.8-42.0 GHz band. The effect was established by different methods, both in suspended cells and in monolayer. According to recent observations [Grundler and Kaiser, 1992], an effect of about the same magnitude is produced by the field intensities from 5 pW/cm2 to 10 mW/cm2 (8 kHz modulation). The width of the resonance peaks increased with the intensity from about 5 MHz to 12-15 MHz for the above intensity range. However, thorough independent attempts to replicate these findings were not successful [Furia et al., 1986; Gos et al., 1997], suggesting that these MMW effects could be dependent on (or even produced by) some yet unidentified and uncontrolled conditions.

Dardanoni and co-authors [1985] observed frequency-and modulation-dependent effects on the growth of yeast *Candida albicans.* MMW modulated at 1 kHz reduced the growth rate by

about 15% at 72 GHz, but not at 71.8 or 72.2 GHz. A 3-hour continuous wave (CW) irradiation at 72 GHz had the opposite effect, i. e., increased the growth rate by about 25% over the sham irradiated control. Remarkable variability of the results was noted, which could be a result of cell subpopulations with different sensitivity.

Golant and co-authors [1994] reported that a marked synchronicity of periodic fluctuations in the growth rate and bud formation in the culture of S. *cerevisiae* can be induced by 0.03 mW/cm2, 46 GHz irradiation for 50 min. This effect was claimed to persist for over 20 cell generations. Periodicity of bud formation was observed in control samples as well, but it was less pronounced and had a different time duration (60 min versus 80 min after MMW exposure).

Synchronizing effects of MMW were also observed in higher plant specimens (Shestopalova et al., 1995). Barley seeds were exposed for 20 min at 0.1 mW/cm2 (61.5 GHz), then the exposed and control seeds (150 seeds per group) were put into an incubator for sprouting. The incubator was maintained at either 28 ^{o}C or 8 ^{o}C. Cytological examination established that the degree of synchronization of cell division in MMW-exposed sprouts increased by 36% (28 ^{o}C) and 50% (8 ^{o}C) over the respective controls.

Levina et al. [1989] studied MMW effects on the development of a Protozoan *Spirostum sp.* cell population. The population began in a saline medium with beer yeast (550 mg/l) as food by adding of 5-6 protozoan cells/ml. The culture was exposed for 30 min at 1.5 mW/cm2 (7.1-mm wavelength), a single time between days 2 and 11 of the growth. Unexposed cultures grew exponentially up to a density of 100 cells/ml on day 11, then rapidly died without reaching stationary phase, obviously due to poisoning by waste products. Exposures performed on days 2, 4, or 7 caused the populations to enter the stationary phase on or around day 9. Exposures performed on day 9 or 11 postponed the population death by 5 days, and the final cell content increased to 115-135 cells/ml on day 14. Irradiation on day 2 also increased the proliferation rate, and by day 7 the cell density was nearly twice as high as in control samples. In another series of experiments, the population began with the initial concentration of 1-2 protozoan cells/ml, and stabilized in 8-10 days at 12-13 cells/ml. In these cultures, MMW exposure suppressed proliferation, and the final cell density was only 6-10 cells/ml. This study indicated that irradiation affects the population's own growth control mechanisms, and that the effect depends on the stage and other particulars of the population development.

Exposure for 30 min at 2.2 mW/cm2, 7.1-mm wavelength enhanced the growth of a blue-green algae *Spirulina platensis* by 50% [Tambiev et al., 1989], while 8.34-mm wavelength produced no changes compared with sham control. The alga growth rate more than doubled when a 30-min irradiation at 7.1-mm was immediately followed by exposure to high-peak power microwave pulses (15 pulses, 10-ns pulse width, 6-min pause, 3-cm wavelength, 200-kW/cm2 peak incident power density). Concurrently, photosynthetic oxygen evolution increased about 1.5 times. The observed stimulatory effects are of considerable promise in biotechnology, where *S. platensis* is used for production of food protein and biologically active compounds.

Other publications by the same authors [Tambiev and Kirikova, 1992] and independent investigators [Rebrova, 1992; Shub et al., 1995] declared observed MMW effects on the growth rate of several species of bacteria, cyanobacteria, algae, yeasts, and higher plants (fennel, lettuce, tomato). For example, in yeasts *S. cerevisiae* and *S. carlsbergensis* MMW shortened the phases of culture growth 2.3-6.0 times, and could increase the biomass production rate to 253%. Effects on *Escherichia coli* growth could be either stimulatory or

inhibitory, depending on the wavelength (6.0-6.7 mm band, £ 1 mW/cm2 for 30 min). However, all three papers were written as summaries of the authors' multiyear experiences with studying these and other MMW effects, and did not provide enough detail for full evaluation or possible replication.

2.2. Chromosome alterations and genetic effects of MMW.

Absence of mutagenic or recombinagenic effects of MMW radiation was clearly demonstrated in the late 1970's [Dardalhon et al., 1979, 1981], and later investigations were consistent with this conclusion. At the same time, a number of studies indicated that MMW could affect the fine chromosome structure and function, cell tolerance to standard mutagens and lesion repairs.

Best known is the recent work by Belyaev and co-authors [1993a, b, 1994, 1996], who discovered sharp frequency resonances by using an anomalous viscosity time dependence (AVTD) technique. This technique is supposed to reflect fine changes in DNA conformation and DNA-protein bonds. At a resonance frequency, biological changes could be produced by field intensities as low as 10-19 W/cm2. The magnitude of changes gradually increased with the field intensity and reached a plateau between 10-17 and 10-8 W/cm2, depending on cell density in exposed samples. Resonance peaks for *E. coli* cells were found at 51.76 and 41.34 GHz; these values decreased in strains with increased haploid genome length. These results pointed to the chromosomal DNA as a target for resonance interaction between living cells and MMW. The width of the resonances increased from units to tens of MHz by increasing the incident power, and this dependence is in a notable agreement with the one reported for cell growth rate effects [Grundler and Kaiser, 1992].

However, the AVTD test is not a conventional technique in cell biology. Interpretation of AVTD data is uncertain and functional consequences of AVTD changes have not yet been convincingly defined. A discussion is going on as to whether super-low radiation intensities in these studies were measured correctly [Osepchuk and Petersen, 1997; see also their letter and Belyaev's reply in one of forthcoming BEM issues]. Supposedly, some power at a harmonic frequency might be transmitted to the sample despite large attenuation at the fundamental frequency. Whether this was the case or not, consistent observations of resonance effects represent an important finding, which requires understanding and independent replication.

MMW induced visible changes in giant chromosomes of salivary glands of the midge *Acricotopus lucidus* [Kremer et al., 1988]. A certain puff, the Balbiani ring BR1 in the chromosome II reduced in size after irradiation at 67,200± 0.1 MHz or 68,200± 0.1 MHz (<5 mW/cm2), and this effect appeared to be unrelated to heating. Numerous alterations in the giant chromosome morphology were also independently found in *Chironomus plumosus* (*Diptera*) after a 15-min exposure at 1 mW/cm2 [Brill' et al., 1993].

Exposure of UV-treated *E. coli* culture to MMW at 61± 2.1 GHz, 1 mW/cm2 increased cell survival [Rojavin and Ziskin, 1995]. The most likely mechanism of this effect was either direct or indirect activation of the dark repair system. No survival effects were found if the sequence of exposures was reversed, i. e., when UV irradiation was performed immediately after a 10- to 30-min MMW exposure.

Genetic effects of 61.02-61.42 GHz radiations were studied in D7 strain of the yeast *S. cerevisiae* [Pakhomova et al., 1997]. MMW exposures lasted for 30 min at 0.13 mW/cm2, and were followed in 60 min by a 100 J/m2 dose of 254 nm UV radiation. Compared with

the parallel control, the MMW pretreatment did not affect cell survival or the rate of reverse mutations, but significantly increased the incidence of gene conversions. Sham-exposed samples showed no differences from respective parallel controls. The data suggested that MMW did not alter the UV-induced mutagenesis, but might facilitate UV-induced recombinagenic processes. Thermal mechanism of this effect was improbable, although could not be ruled out entirely.

2.3 Excitable tissues and membranes

Along with the genetic apparatus, the cell membrane is another site suspected to be a primary target for MMW radiation. Many of the works discussed below established profound MMW effects; however, only a few attempts have been made to replicate them.

Brovkovich et al. [1991] reported that 61 GHz, 4 mW/cm2 radiation significantly activates the Ca^{++} pump in the sarcoplasmic reticulum (SR) of skeletal and heart muscles of the rat. The rate of Ca^{++} uptake by SR membranes was measured by an ion-selective electrode in an ATP-containing medium. An intermittent MMW treatment (5 min exposure, 15 min pause, 3 cycles) of skeletal muscle SR increased the rate of Ca++ uptake by 23%, and this increased level has retained for one hour after the exposure. Uninterrupted MMW irradiation had no effect in 10 min, but increased Ca^{++} uptake by 27% in 20 min, and the effect reached maximum (48%) in 40 min. In heart muscle SR, even a 5-min exposure enhanced Ca^{++} uptake by 18%.

Geletyuk and co-authors [1995] used patch-clamp (inside-out mode) to study 42.25 GHz radiation effects on single Ca^{++}-activated K^{+} channels in cultured kidney cells (Vero). Exposure for 20-30 min at 0.1 mW/cm2, CW, greatly modified the activation characteristics of the channels, in particular, the open state probability. The field increased the activity of channels with a low initial activity, and inhibited channels with initially high activity. In a subsequent study [Fesenko et al., 1995], these effects were reproduced without direct irradiation of the membrane, just by applying bathing solution pre-exposed for 30 min at 2 mW/cm2, 42.25 GHz. Irradiation of the solution did not alter its pH or Ca^{++} concentration, and the nature of the MMW-introduced channel-modifying properties of the solution is not understood. The solution retained its biological efficacy for at least 10-20 min after cessation of the exposure.

Kataev and co-authors [1993] used voltage clamp to study membrane currents in giant alga cells (*Nitellopsis obtusa, Characea*). Irradiation for 30-60 min at 41 GHz, 5 mW/cm2 suppressed the chloride current to zero with no recovery for 10-14 hours. Marked inhibitory effects were also found at 50 and 71 GHz, while most of other tested frequencies in 38-78 GHz range enhanced the chloride current up to 200-400% (49, 70, 76 GHz). This activation was reversible, and recovery to the initial value took 30-40 min. Moreover, "activating" frequencies could restore the chloride current after its complete and normally irreversible suppression by "inhibitory" frequencies. MMW heating did not exceed 1 ^{o}C, and neither activating nor inhibitory effects were related to, or could be explained by it. Calcium current also changed during irradiation, but this effect was not frequency-dependent and could be adequately explained by heating. The authors noted that algae collected in the fall of 1990 and stored over the winter have entirely lost MMW sensitivity by February 1991.

Experiments with artificial bilayer membranes and snail neurons did not reveal any frequency-specific effects of MMW [Alekseev and Ziskin, 1995; Alekseev et al., 1997]. The capacitance of artificial membranes, ionic channel currents, and the transport of tetraphenylboron anions changed proportionally to MMW heating, regardless of the

frequency (53-78 GHz range) or modulation employed. Irradiation of snail neurons at 75 GHz (600 to 4,200 W/kg) produced biphasic alterations of their firing rate, which were similar to those caused by equivalent conventional heating.

Burachas and Mascoliunas [1989] studied MMW effects on the compound action potential (CAP) in isolated frog sciatic nerve.. CAP decreased exponentially and fell tenfold within 50-110 min of exposure at 77.7 GHz, 10 mW/cm2. CAP restored entirely soon after the exposure, but the nerve became far more sensitive to MMW: CAP suppression due to the next exposures became increasingly steep and finally took only 10-15 min. This sensitized state persisted for at least 16 hours. In addition to this "slow" response, switching the field on increased CAP amplitude instantly by 5-7%, and switching it off caused the opposite reaction. These effects were found in "winter" frogs, but weakened and finally disappeared in spring.

A different effect in the isolated frog nerve was described by Chernyakov and co-authors [1989]. The exposures lasted for 2-3 hours, either with a regular frequency change by 1 GHz every 8-9 min, or with a random frequency change every 1-4 min (53-78 GHz band, 0.1-0.2 mW/cm2). The latter regimen induced an abrupt CAP "rearrangement" in 11 out of 12 exposed preparations: the position, magnitude, and polarity of CAP peaks (the initial CAP was polyphasic) drastically changed in an unforeseeable manner. The other exposure regimen altered the amplitude and duration of late CAP components in 30-40 min. The authors supposed that MMW increased CAP conduction velocity in fast nerve fibers and decreased it in slow fibers.

Neither of these effects on CAP conduction was observed by Pakhomov et al. [1997a]. Irradiation for 10-60 min either at various constant frequencies, or with a stepwise frequency change did not alter CAP at 0.2-1 mW/cm2. At 2.0-2.8 mW/cm2, it produced minor changes, which were independent from the frequency and matched the effect of heating. At the same time, a different MMW effect was revealed using a high-rate nerve stimulation test. MMW attenuated the stimulation-induced CAP decrease in a frequency-dependent manner. The effect reached maximum at 41.34 GHz [Pakhomov, 1997b], and at this frequency the magnitude of changes was the same (20-25%) at 0.02, 0.1, and 2.6 mW/cm2 [Pakhomov et al., 1997c]. A 100-MHz deviation from 41.34 GHz (to 41.24 or 41.44 GHz) reduced the effect about twofold, and a 200-MHz deviation eliminated it. The field distribution over the preparation at these frequencies was virtually the same, so different MMW absorption or heating patterns could not account for the frequency-specificity of the effect. Interestingly, the most effective frequency in these experiments happened to be the same as the resonance frequency in the cell genome studies of Belyaev et al. [1993a].

Low-intensity MMW radiation effectively changed membrane functions in striated muscle and cardiac pacemaker cells [Chernyakov et al., 1989]. Exposure at 0.1-0.15 mW/cm2 for 90 s or less (frequencies between 54 and 78 GHz) decelerated the natural loss of transmembrane potential in myocytes, or even increased it by 5-20 mV. Exposure reduced the overshoot voltage, action potential amplitude and conduction velocity. This effect was observed in 80% of exposures, with no clear dependence on the radiation frequency. MMW influence on pacemaker activity was analyzed in 990 experiments with 80 tissue strip preparations from the frog heart sinoatrial area. In most cases, irradiation immediately (often in less than 2 s) decreased the interspike interval. The maximum effect was reached within 30 s. The changes linearly increased with the incident power increase in the range from 20-30 to 500 m W/cm2. The frequency dependence of the effect was individual, with at least four maximums in the studied range. Maximum preparation heating after a 2-s

exposure at 1 mW/cm2 was calculated as 0.005 °C. With a physiological response latency of less than 2 s, this response could not be thermal. Exposure to infrared light (4- to 6-m m wavelength) often evoked the same effects as MMW, but the threshold intensity was hundreds times greater.

In other experiments described in the same paper, low-intensity MMW synchronized firing of urinary bladder mechanoreceptors; suppressed and altered the T-peak of EKG of *in situ* exposed myocardium; enhanced respiration, altered membrane calcium binding, and reduced the contractility of cardiomyocytes. Summarizing their results, the authors stated that the dependence of bioeffects upon radiation frequency is not monotonic. Peaks of this dependence are individual and are not fixed at particular frequencies, and they become smoother with increased complexity of physiological control mechanisms involved.

2.5 Other *in vitro* effects

Bulgakova et al. [1996] studied how MMW exposure of *S. aureus* affects its sensitivity to antibiotics with different mechanisms of action. Irradiations lasted from 1.5 to 60 min (54 or 42.195 GHz, or 66-78 GHz band with 1 GHz steps, ³ 10 mW/cm2). MMW heating did not exceed 1.5 °C. Over 1,000 experiments with 14 antibiotics were completed. A difference in the growth of exposed cells compared to controls was most often observed with polypeptide antibiotics, which affect the cell membrane (gramicidin group), but not with inhibitors of cell wall synthesis (penicillin group), of DNA-dependent RNA synthesis (actinomycin D), of the RNA polymerase and RNA synthesis (heliomycin), or protein biosynthesis inhibitors (neomycin, tetracycline, etc.). Irradiation either increased or decreased the antibiotic sensitivity, and the probability of these opposite effects depended on the antibiotic concentration. MMW could induce sensitivity to sub-bactericidal antibiotic concentrations, which normally would not affect the cell growth. Within studied limits, the effect showed no clear dependence on the radiation intensity or frequency. The data suggested that some membrane processes might be a target for the MMW effect. The authors also noted that MMW treatment can reveal (or even induce) the heterogeneity of the sensitivity of a cell population to certain antibiotics.

Rebrova [1992] reviewed various MMW effects on cell metabolism, synthesis of enzymes, and other processes in unicellular organisms, e.g., frequency-dependent enhancement and suppression of colicin synthesis in *E. coli*, stimulation of synthesis of fibrinolytic enzymes in *Bacillus firmus,* increasing of the contents of peptides, DNA, and RNA in *B. mucilaginous*, and suppression of tolerance to antibiotics in *Staphylococcus aureus*. The maximum magnitude of MMW-induced changes ranged from 20 to 90%, depending on the wavelength and the initial condition of the strain. In contrast to bacteria, reproduction rate and biosynthetic properties of fungi *Aspergillus sp*., *Endomyces fibuliger*, and *Dacthilyum dendraides* changed only after repeated exposures (10 times). Certain MMW frequencies increased alpha amylase activity in *A. orizae* by 67% and suppressed glucoamylase by 30%; others had the opposite effect. In yeast species, MMW accelerated maltose fermentation by 73%, while synthesis of diacetil and aldehydes decreased by 20%. New biosynthetic culture properties introduced by exposure persisted in at least 100 (*S. carlsbergensis*) and 300 (*S. cerevisiae*) cell generations. The selective stimulation of production of some enzymes and suppression of others is promising for biotechnology.

An unusual "double-resonance" effect of MMW was described by Gapeev et al. [1994]. Spontaneous locomotor activity of the Protozoan *Paramecium caudatum* was not affected by irradiation unless both the radiation frequency and modulation were tuned to "resonance" values. These values were 42.25 GHz and 0.0956 Hz, respectively (0.5 duty ratio). At these

parameters, the threshold field intensity was about 0.02 mW/cm2. The effect reached maximum (about 20%) at 0.1 mW/cm2, and remained at this level at intensities up to 50 mW/cm2, despite increasing heat production (0.1-0.2 °C at 5 mW/cm2). CW irradiation or modulation rates of 16, 8, 1, 0.5, 0.25, or 0.05 Hz produced no effect, regardless of the field intensity or heating. At the resonance modulation frequency, a shift of the carrying frequency to 42.0 or 42.5 GHz eliminated the reaction. No effects were observed with heating of samples by other means, e.g., infrared light modulated at 0.0956 Hz. Locomotor activity changes similar to the MMW effect could be evoked by increasing the level of intracellular calcium, pointing to a possible mechanism of the MMW action. However, reasons for the "double-resonance" dependence of this MMW effect remain unclear.

More reported MMW effects in various *in vitro* systems are summarized in Table 1.

3. ANIMAL AND HUMAN STUDIES

3.1. MMW effects on peripheral receptors

Abundant evidence for MMW effects in directly exposed specimens neither explains nor predicts possible effects at the organism level. It is clearly understood that MMW penetration into biological tissues is rather shallow, and any primary response must occur in skin or subcutaneous structures, or at the eye surface. This primary response would then mediate all subsequent reactions via neural and/or humoral pathways. The nature of the primary response and consequent events has been a subject of intense speculation [Golant, 1989; Mikhno and Novikov, 1992; Rodshtadt, 1993], but there is little experimental proof. As a matter of fact, the link between cellular and organism effects is missing and remains the least understood area in the MMW field. However, several studies have suggested that peripheral receptors and afferent nerve signaling could be involved in the whole organism's response to a local MMW exposure.

Akoev et al. [1992] studied the response of electroreceptor Lorencini capsules in anesthetized rays. Spontaneous firing in the afferent nerve fiber from the capsule could be either enhanced or inhibited by MMW irradiation (33-55 GHz, CW). The most sensitive receptors increased their firing rate at intensities of 1-4 mW/cm2, which produced less than 0.1 °C temperature rise. Intensities of 10 mW/cm2 and higher could evoke a delayed inhibition of firing, so the response became biphasic. The authors emphasized that what they observed was not merely a bioeffect of MMW, but was indeed a specific response of the receptor.

Chernyakov and co-authors [1989] were able to induce heart rate changes in anesthetized frogs by MMW irradiation of remote skin areas. The latency of the changes was about 1 min. Complete denervation of the heart did not prevent the reaction, but decreased its probability. The data suggested a reflex mechanism of the MMW action, maybe involving certain peripheral receptors.

These data are in agreement with later findings by Potekhina et al. [1992]. Certain frequencies from 53-78 GHz band (CW) effectively changed the natural heart rate variability in anesthetized rats. The radiation was applied to the upper thoracic vertebrae for 20 min at 10 mW/cm2 or less. The frequencies of 55 and 73 GHz caused pronounced arrhythmia: the variation coefficient of the R-R interval increased 4-5 times. Exposure at 61 or 75 GHz had no effect, and other tested frequencies caused intermediate changes. Skin and whole-body temperature of the animals remained unchanged. Similar frequency dependence was observed in additional experiments with 3-hour exposures; however, about 25% of

experiments were interrupted because of sudden animal death that occurred after 2.5 hours of exposure at 51, 61, and 73 GHz. Possible role of receptor structures and neural pathways in the development of the MMW-induced arrhythmia was discussed.

Sazonov et al. [1995] compared alterations of spontaneous afferent firing in bladder nerve in frogs when the bladder was exposed to infrared radiation and to MMW (42.19 ± 0.15 GHz, 10 mW/cm2). The infrared intensity was adjusted to produce the same heating as MMW. In control experiments, the firing rate was stable for at least 1-1.5 hours, but MMW increased it instantly from 30.9 to 32 spikes/s ($p<0.05$), and to 48.3 spikes/s ($p<0.01$) by the end of a 20-min exposure. Immediately after cessation of irradiation, the rate fell to 35.8 spikes/s, which was still significantly higher ($p<0.05$) than before the treatment. Infrared irradiation did not cause statistically significant changes. This difference was interpreted as a proof of a specific (nonthermal) MMW effect, which, in principle, might take place in skin receptors as well.

In contrast, infrared light and MMW at equivalent intensities produced similar effects on the firing rate of crayfish stretch receptor [Khramov et al., 1991]. Changes were proportional to the average incident power, regardless of modulation or radiation frequency, and were regarded as merely thermal.

The possibility of modifying the peripheral receptor function by low-intensity MMW has been demonstrated directly by Enin and co-authors [1992]. An electrodynamic mechanostimulator was used to apply mechanical stimuli (50 ms duration, 1-2 mm amplitude) to individual skin mechanoreceptors on the sole of the hind limb of anesthetized rats. Responses to the stimuli were recorded from afferent fibers in the isolated and cut peripheral end of the tibial nerve. The sole was exposed to 55-, 61-, or 73-GHz radiation at 0.75, 2.90, or 7.81 mW/cm2, respectively. Exposure lasted for 35 min and caused no changes in the skin temperature (0.01 ^{o}C accuracy). MMW did not excite mechanoreceptors, but markedly altered the threshold and latency of their response to mechanic stimuli. In some receptors, the threshold gradually increased, up to 180% of the initial value. In others, the threshold initially decreased by 8-12%, recovered within 10 min, and increased to 160% by the 25th min of irradiation; after that, the receptors became completely inactive and no longer responded to mechanical stimuli. The receptor response latency under exposure could fall to 70%, or rise to 120%, or the changes were biphasic. The MMW-induced changes were maximum at 73 GHz, intermediate at 55 GHz, and minimum at 61 GHz, despite the fact that the incident power at 61 GHz was 4-fold greater than at 55 GHz. The authors supposed that sensations reported by patients under MMW therapy (vibration, warmth, numbness, etc.) may result from functional disturbances and blockage of receptors.

The ability of humans to detect weak MMW has also been repeatedly established under double-blind conditions [Lebedeva, 1993, 1995; Kotrovskaia, 1994]. An examinee was situated in an isolated room and had no contact with the experimenter. The outer surface of the hand was exposed 20 times, for 1 min each. Exposures were separated by 1-min intervals and randomized with sham exposures. The start and end of each irradiation and placebo were accompanied by sound clicks. The examinee had to push a button when he felt the field. Neither examinee nor researcher knew the sequence of exposures and sham exposures; correct and incorrect reactions were recorded automatically. Field perception was characterized by the reaction reliability (the percent of MMW exposures detected) and the false alarms level (the percent of sham exposures erroneously detected). An examinee was regarded as capable of detecting the field if the reaction reliability consistently and statistically significantly exceeded the false alarm level. With different frequencies (37.7,

42.25, 53.57 GHz), intensities (from 5 to 15 mW/cm2) and bandwidths, the radiation was detected by 30 to 80% of examinees. Interestingly, 37.7 GHz radiation at 15 mW/cm2 was detected by far fewer people than 42.25 GHz at 5 mW/cm2. The reaction latency was usually between 40 and 50 s. It was speculated that MMW perception could involve some types of mechanoreceptors and nociceptors.

3.2 Teratogenic effects of MMW

The only study of MMW teratogenic effects was performed in *Drosophila* flies by Belyaev et al. [1990]. Embryos of the blastula and gastrula stages (2.5-3 hours after laying) and pupas at the stage of imago tissue formation were exposed in a waveguide at 46.35, 46.42, or 46.50 GHz, for 4-4.5 hours at 0.1 mW/cm2, followed by incubation at 25 ^{o}C. Irradiation at 46.35 GHz, but not at 46.42 or 46.50 GHz, caused marked effects. Exposure of pupas increased incidence of morphological abnormalities 2-4.5 times ($p<0.05$), but did not influence imago survival. Exposure of embryos decreased survival by about 30% ($p<0.05$) and enhanced morphological abnormalities, but this effect was rather variable. Supposedly, MMW disturbed DNA-protein interactions which determine the realization of the ontogenetic program.

3.3 High-power MMW effects

Over the past several years, physiological effects of high levels of MMW radiation have been intensively studied by Frei et al. [1995], Frei and Ryan [1995], and Ryan et al. [1996, 1997]. In ketamine anesthetized rats, exposure to 35 GHz, 75 mW/cm2 radiation (12-13 W/kg whole body SAR) increased the subcutaneous temperature by 0.25 ^{o}C/min and the colonic temperature by 0.08 ^{o}C/min. Concurrently with the hyperthermia, mean arterial blood pressure first increased slightly and then fell until the point of death. Hypotension was accompanied by vasodilatation in the mesenteric vascular bed, which was similar to heat stroke induced by environmental heating. However, the onset of vasodilatation and hypotension occurred at much lower colonic temperatures (< 37.5 ^{o}C versus > 41.5 ^{o}C). The lethal effect became irreversible when the mean arterial pressure fell to 75 mm Hg, even if the exposure was discontinued. Most intriguing, pathological examination of the skin of lethally exposed animals revealed no significant thermal damage or full-thickness burn, and cardiovascular responses did not mimic those observed in traditional burn models. Searching for physiological mechanisms mediating the hypotensive response, the authors established that nitric oxide, platelet-activating factor, and histamine do not contribute to it. Exposure of rats at 94 GHz at a similar SAR produced a comparable pattern of heating and cardiovascular responses.

3.4 Experimental MMW therapy: animal studies.

Except those cited above, virtually all animal studies on MMW effects have been related to various issues of MMW therapy, such as stress relief, wound healing, tissue regeneration, and protection from ionizing radiations. Paradoxically, these animal studies are still less numerous and comprehensive than reports on MMW therapy in humans. Many applications of the MMW therapy seem to have never been adequately tested in animal experiments. For example, we counted 38 publications (including meeting abstracts) on various clinical aspects of the MMW therapy for peptic ulcers, but could find just one animal study on this subject. It appears that, in some cases, animal studies did not precede the clinical use of MMW (as one would expect), but were carried out to create experimental justification for already reported clinical data.

3.4.1 Tissue repair and regeneration. Among possible therapeutic applications of MMW, the more plausible and understandable is treatment of surface lesions (wounds, burns, ulcers), which are directly reachable by the radiation. Indeed, this application has gained sound experimental support in several independent works. Other studies have demonstrated that repair of deep tissues (bone and nerve) could also be stimulated by MMW, suggesting that such effects are mediated by activation of the organism's own recovery mechanisms.

Zemskov et al. [1988] studied MMW effects on healing of skin wounds in rabbits. The animals were randomly assigned to four groups; wounds in groups 1 and 2 were kept aseptic, and in groups 3 and 4 were infected with a pathogenic *Staphylococcus*. The wound surface in groups 1 and 3 was treated with 37 or 46 GHz CW MMW at 1 mW/cm2 for 30 min twice a day, for 5 days. A horn irradiator was placed 2-5 mm over the wound surface. Rabbits in groups 2 and 4 served as untreated controls. MMW decreased swelling of wound edges, hyperemia, and infiltration, and rapidly reduced the wound area in the first 24 hours; it also stimulated phagocytosis and reduced bacterial contamination. Complete healing of aseptic wounds in the exposed group took 2.9 days less than in the control group. Infected wounds cleaned up and filled with granulation tissue on days 14-16 in the exposed group, and only on days 21-23 in the respective control.

A similar protocol was employed in a double-blind replicative study by Korpan et al. [1994]. Rabbits with 4 x 6 cm cutaneous wounds were randomly divided into 4 groups of 18 animals each. The wounds of two groups were rendered septic by inoculating them with 10^9 *Staphylococcus* cells. The wound was exposed for 30 min a day (37 GHz CW, 1 mW/cm2), for 5 days in one aseptic group and for 7 days in a septic one. The horn aperture was 10 cm from the wound surface. The other two groups were sham-irradiated and served as aseptic and septic controls. In irradiated animals, wound edge swelling and hyperemia subsided faster, and granulation tissue filled the wound earlier. On day 7, for example, the surface area of septic wounds decreased by 19% in the control group, and by 44% in the irradiated group. The mean daily decrease in wound surface area of the irradiated animals was significantly greater than in the controls: 7.9% versus 3.2% in the aseptic groups, and 6.3% versus 2.7% in the septic groups ($p<0.05$). Exposures stimulated phagocytic activity of neutrophils and decreased the blood level of circulating immune complexes. Thus, MMW irradiation enhanced both septic and aseptic wound healing and stimulated immune function.

Detlavs et al. [1993, 1994, 1995, 1996] have extensively studied MMW effects on the composition of granulation fibrous tissue (GFT) during early stages of wound healing. Their experiments were performed in rats with incised full-thickness dermal wounds. The injured area was exposed for 30 min daily for 5 days at 10 mW/cm2 (53.53 or 42.19 GHz CW, or 42.19 GHz with ± 200 MHz frequency modulation). Control animals underwent the same manipulations, but were sham exposed. GFT samples from the wound were taken for analysis on the 7th day. CW irradiation significantly decreased the GFT contents of glycoproteins (hexosamines, hexoses, and sialic acids), indicating a suppression of the inflammatory process. In contrast, modulated MMW enhanced the inflammation and increased the production of glycoproteins. CW exposure decreased the GFT content of hydroxyproline, which is a marker for total collagen, to 79-85% of the control ($p<0.01$), while the modulated regimen increased it to 126-133% ($p<0.001$). CW radiation at 53.53 GHz usually was more effective than at 42.19 GHz. Both the anti- and pro-inflammatory effects of MMW could be useful in clinical practice. CW exposure can be recommended for early stages of the wound healing when control of the inflammatory reaction is desirable. Modulated radiation can be used to promote ultimate recovery in slow-healing wounds, or in cases of healing deceleration in the late stages of tissue repair.

Ragimov et al. [1991] used MMW to stimulate the repair of an experimentally produced bone defects in rabbits. A hole 6 mm in diameter was drilled in the lower jaw bone, and the wound was sutured. The first exposure for 30 or 60 min was performed the next day, and six more exposures were done over the next two weeks. The shaven nape was exposed from a horn (2-cm2 aperture) placed 3-4 mm from the skin (5.6 mm wavelength, 25 mW output power). Control animals were handled similarly. Five animals from each group were killed every week for morphological and roentgenographic analysis of bone repair. One week after the operation, the extent of reparative osteogenesis was the same in all the groups. Later on, the regeneration was faster in exposed animals, particularly in the group with 60-min exposures. By the end of the observation period (28 days), the appearance of the traumatic defect in the control group was nearly the same as it was in exposed animals on day 21. Hence, irradiation shortened the bone repair time by approximately one week.

Kolosova and co-authors [1996a] established that MMW treatment could promote regeneration of a damaged peripheral nerve. The sciatic nerve in 40 rats was transected in the thigh region and sutured. Skin over the injury area was irradiated every third day for 10 min with 4-mW/cm2, 54-GHz radiation for 7 or 20 days; control rats were sham irradiated. Exposures did not change the skin temperature (0.1 ^{o}C accuracy). Upon the completion of the treatment course, the nerve was isolated, and the extent of regeneration was assessed electrophysiologically. After the 7-day course, the regeneration distance was 4.8 mm versus 3.0 mm in the controls ($p>0.05$). After the 20-day course, the effect became statistically significant: the regeneration distance was 18.4 ± 0.4 mm versus 14.0 ± 1.4 mm ($p<0.01$). The nerve conduction velocity also significantly increased, while the amplitude and duration of the action potential were not affected.

In a continuation study [Kolosova et al., 1996b], the same irradiations were performed for two weeks after the injury, and the nerve was isolated for examination in 5 months. Indices of regeneration were the compound action potential amplitude and conduction velocity at different distances (5 to 19 mm) distal from the suture. Both parameters were higher in the exposed animals. For example, 19 mm from the suture, the velocity was 20.4 ± 0.9 m/s versus 15.5 ± 0.9 m/s in controls ($p<0.05$), and the amplitude was 313 ± 34 m V versus 156 ± 15 m V ($p<0.001$). Hence, exposures not only stimulated the growth of nerve fibers, but facilitated their functional maturation as well.

3.4.2 Tumor growth and development. Experiments by Smirnov et al. [1991] were designed to evaluate the possible use of MMW for the treatment of cancer. VMR tumor cells with a high metastasizing activity were inoculated into the tibial muscle of A/SNL line mice at 5 x 105 cells/animal. Exposure for 5 days, one hour daily (12.5 mW/cm2, 7.09-7.12 mm wavelength, 50 Hz modulation), increased the average life span by 17% compared with sham controls. The number of visible metastases decreased by more than 50% in lungs, liver, kidney, and adrenal glands, but not in lymph nodes. The authors noted variability of the MMW effect, and, in one series, exposure even intensified metastasizing.

Chernov et al. [1989] attempted to suppress malignant growth by extremely-high peak power nanosecond MMW pulses. Rats were exposed immediately after inoculation with 10, 25, or 50 (x 103) Walker tumor cells, and two more times during the next two days. Each exposure consisted of 43 pulses delivered with 40-s intervals. Two regimens were tested: 8 mm wavelength at 4-5 MW output power, yielding 20 kV/cm E-field level at the skin surface, and 5 mm, 8-10 MW, 30 kV/cm, respectively. The first of these regimens retarded tumor growth 1.5 times and increased the life span by 17-25 days after the doses of 10 and 25 (x 103); the other regimen was less effective. The antitumor effect was presumably mediated by stimulation of immune system, namely the so-called skin-associated lymphoid

tissue. Preliminary studies with exposure prior to tumor inoculation showed that MMW retarded the tumor growth nearly twofold.

Because of concern about possible adverse effects of MMW use in cancer patients, Brill' and Panina [1994] studied the transplantability and growth of a benign tumor (mammary fibroadenoma) in rats. Two tumor pieces were implanted to the right and left sides through a cut in the middle of the abdomen. In 20 of 49 operated animals, tissues in the cut were exposed to MMW (42.0-43.3 GHz band) for 15 min before the implantation, the other animals served as control. In 3 weeks, 39 out of 58 tumors (67.3%) resolved in the control group, but only 11 out of 40 (27.5%) resolved in the exposed animals ($p<0.001$). The percentages of stable and growing unresolved tumors in both the groups were the same. Hence, a single MMW exposure of the implantation area increased tumor transplantability, though did not affect its proliferation.

3.4.3 Stress alleviation and prevention effects. Temur'iants and Chuyan [1992] demonstrated that MMW can alleviate immobilization-induced stress in rats. The authors established that this MMW effect differed in specimens with different characteristic levels of exploratory activity, as evaluated by an open-field testing. In further studies, the open-field testing was always done prior to stressing and MMW exposures, to divide the population into appropriate groups.

One of these studies [Temur'iants et al., 1993] was performed on 350 animals divided into groups with a low (LA), medium (MA) and high (HA) activity. Each group was subdivided into 5 groups; group 1 was cage control, and groups 2-5 were housed for 9 days in individual boxes restricting their motion. Animals in groups 3-5 received daily 30-min MMW exposures of the occipital area, left hip, or right hip, respectively (5.6-mm wavelength, 10 mW/cm2). Stress severity was quantified by indices of the "nonspecific resistivity" of the organism, which included the contents of lipids and peroxidase in neutrophils, and activities of succinate and alpha-2-glycerophosphate dehydrogenases in lymphocytes. A typical stress reaction developed in unexposed MA rats: by days 6-9, the contents of lipids and peroxidase decreased by 21-24%, and the activity of dehydrogenases fell by 36-46%. Occipital or right hip MMW irradiation prevented the stress reaction in MA rats, while the left hip exposure was not effective. The immobilization stress was the most pronounced in unexposed HA animals; MMW exposures of the left hip or occipital area prevented stress, while exposures of the right hip had little effect. In LA animals, the stress reaction was relatively weak, and all the types of MMW treatment alleviated it.

The next study employed 640 albino rats, all with a medium level of locomotor activity [Temur'iants et al., 1994]. The same indices as above were compared in four groups: cage control, hypokinesia without exposures, exposures without hypokinesia, and both. Occipital area was exposed for 30 min/day, 9 days at either 5.6 or 7.1 mm wavelength. Exposures without hypokinesia strongly activated succinate dehydrogenase (up to twofold, $p<0.05$). Irradiation at 5.6 mm (but not at 7.1 mm) increased the activities of acid and alkaline phosphatases and glycerophosphate dehydrogenase by 20-30%. Both wavelengths prevented or reversed stress-induced changes, 5.6 mm was more effective. Further experiments with 5.6 mm radiation established that exposures for 15 min/day were less effective than for 30 min/day, and, paradoxically, increasing the exposure duration to 60 min/day eliminated its anti-stress effect.

A similar exposure technique was independently used by Arzumanov et al. [1994]. The occipital area was exposed at 5.6 mm simultaneously with immobilization of the rat's head for 60 min/day for 10 days. This stressing suppressed feeding and sexual behavior, and

increased the motor activity in a swimming test to the same degree in exposed and unexposed groups. The authors hypothesized that the immobilization stress was too severe and might mask MMW effects, so in the next series rats were immobilized and exposed for only 30 min/day for 9 days. The stress effect was assessed by the electric shock threshold, free-access water consumption, and Vogel's choice test (consumption of water when each attempt to drink is accompanied by an electric shock). Immobilization without exposure decreased threefold the number of attempts to drink in Vogel's test; but, when immobilization was combined with MMW exposures, this index remained the same as in cage controls. The shock threshold and free-access water consumption were not changed by MMW.

It is interesting to note some parallelism in the above two studies. Using the same exposure procedures, but different protocols and endpoints, both research groups established that there is an anti-stress effect of a 30-min irradiation, but there is no such effect if the exposure duration is 60 min. The decreased efficacy of a more prolonged MMW irradiation has been observed in some other clinical and experimental studies as well, but this unusual time dependence has not been discussed or explained yet.

3.4.4. Combined MMW and ionizing radiation exposure. Gubkina et al. [1996] researched whether low-intensity MMW can alleviate the effect of X-rays in rats. The abdominal area was shaved and exposed to MMW in a frequency-sweep regimen (38 to 53 GHz) at 7 mW/cm2 for 23 days, 30 min/day. Controls not treated by MMW underwent all the same manipulations, including shaving. Exposures to 150 keV X-rays were performed daily during the last 8 days of the MMW course up to a total dose of 24 Roentgen. Blood serum and brain tissue samples were collected the next day after the end of exposures. MMW alone did not alter the serum glucose level (6.24± 0.79 mM versus 6.53± 0.80 mM in controls); X-ray exposure increased it to 10.37± 0.75 mM ($p<0.05$), but combining X-rays with MMW prevented this rise (6.81± 0.37 mM). MMW decreased the content of the soluble form of the acidic glial fibrillar protein (s-AGFP) 1.5-2 times ($p<0.05$) in all analyzed structures of the brain (cerebellum, midbrain, and medulla oblongata), and did not change the content of its fibrillar form (f-AGFP). X-rays decreased the levels of both forms of the protein 2-3 times. After combined treatment with MMW and X-rays, both s- and f-AGFP levels did not differ from controls, and were significantly ($p<0.05$ and $p<0.01$) higher than after X-rays only. The authors concluded that MMW alleviated the effect of X-rays at both cellular and organism levels.

Two other studies are of interest, although they are only brief reports that do not contain essential experimental details. Kuzmanova and Ivanov [1995] studied changes in the surface electrical charge of erythrocytes after MMW and g -ray exposures in rats. The shin of the right hind limb was exposed to 5.6 mm radiation for 10 days, 20 min/day at 1.1 mW/cm2, followed with a 6 Gy whole-body dose of ^{137}Co g -rays. The surface charge of erythrocytes was assessed from their electrophoretic mobility (EPM) 3, 7, 14, 21, and 30 days after the exposures. The MMW treatment alone had practically no effect, while g -rays alone decreased EPM for the whole period of observation. When g -irradiation was preceded by MMW, the EPM remained the same as in controls. The authors concluded that MMW stabilized the membrane structure and increased its resistivity to g -radiation.

Tsutsaeva et al. [1995] examined MMW-induced survival changes in mice after a lethal dose of X-rays. Irradiation with pulse-modulated MMW at 1 m W/cm2 continued for 80 or 24 hours prior to X-ray exposure, or was simultaneous with the X-ray exposure. All tested X-ray doses (7, 7.5, and 8 Gy) were 100% lethal, with the average life span of 6-8 days; the first fatalities occurred on days 4-6. MMW treatment for 80 hours before 7 Gy of X-rays

delayed the first deaths until day 14; 50% of the population died within 30 days, and 100% of the animals died by day 96. The MMW treatment for 24 hours appeared even more effective: first deaths occurred on day 8, 50% of the animals died within 30 days, but no more fatalities were observed through day 96. Microwave irradiation simultaneously with the X-rays (7 Gy) increased the survival and life span of mice approximately 5-fold. The protective effect of 24-hour MMW pretreatment decreased with increasing X-ray dose to 7.5 Gy, and became insubstantial at 8 Gy.

3.5 MMW therapy: clinical studies.

The first clinical trials of MMW therapy began in 1977, and nowadays the method has been officially approved by the Russian Ministry of Health and is used widely. As mentioned in the "Introduction" section, by 1995 over 3 million people have been treated at more than a thousand specialized centers as well as at regular hospitals [Lebedeva and Betskii, 1995].

3.5.1 General issues of the MMW therapy. MMW therapy involves repetitive local exposures of certain body areas with low-intensity MMW. The area(s) to be exposed, the radiation wavelength, and daily duration of procedures are determined by the physician based on the disease and the condition of the particular patient. The radiation intensity is usually regarded as a less important variable. For most diseases, the daily exposure varies from 15 to 60 min, and the therapy lasts for 8-15 days.

Publications on the clinical use of MMW are counted by hundreds, and many of them have claimed that MMW monotherapy is more effective (sometimes, far more effective) than conventional methods, such as drug therapy, for a variety of diseases and disorders. In some cases, MMW has helped the patients who had already tried all other known therapies without success, and were considered incurable. At the same time, MMW seldom caused any adverse effects or allergies. MMW in combination with drug therapy facilitated favorable effects and/or reduced adverse side effects of drugs. Some authors reported that MMW might be highly effective or not effective at all, contingent on the patient's condition, individual sensitivity to MMW, and parameters of irradiation. A few authors reported that MMW therapy was always less effective than conventional techniques, and we found only one clinical study saying that MMW therapy was not effective at all [Serebriakova and Dovganiuk, 1989].

Diseases reported to be successfully treated with MMW belong to rather diversified groups. The most common applications of MMW are for gastric and duodenal ulcers (about 25% of studies), cardiovascular diseases, including angina pectoris, hypertension, ischemic heart disease, infarction (about 25%), respiratory sicknesses, including tuberculosis, sarcoidosis, bronchitis, asthma (about 15%), and skin diseases, including wounds, trophic ulcers, burns, atopic dermatitis (about 10%). These percentages are approximate, because we could not cover all clinical studies published, and because many authors reported treatment of several diseases in one paper (so the sum would be over 100%). Isolated studies claimed successful MMW treatment for asthenia, neuralgia, diabetes mellitus, osteochondrosis, acute viral hepatitis, glomerulonephritis, alcoholism, etc. MMW were also used for alleviation of toxic effects of chemotherapy in cancer patients, and in preventive medicine and health resort therapy.

In most cases, physicians use specialized MMW generators, which are produced commercially by the medical equipment industry. These generators operate at average radiation intensities of 10 mW/cm2 or less, in CW or frequency-modulated regimens, at certain fixed frequencies, or within a wide frequency band. Three models have been used

more often than all others together: "Yav'-1-7,1" (7.1 mm wavelength, 42.19 GHz), "Yav'-1-5,6" (5.6 mm, 53.53 GHz), and "Electronica-KVCh" (4.9 mm, 59-63 GHz band). The respective rates of using these devices are 36%, 31%, and 10%. Different generators were often used within a single study to compare their therapeutic efficacy, and more often than not, the efficacy was different, depending on the disease and patients' condition. Some authors used *in vitro* tests to determine which wavelength is more suitable for a particular patient before the onset of the therapy [Novikova et al., 1995]. However, we have been unable to identify references to the original studies that had shown why the frequencies of 42.19, 53.53, and 59-63 GHz (and not others) should be used for therapy.

In about 30% of clinical studies, the radiation is applied to standard acupuncture points or so-called biologically-active points. This procedure is often combined with finding the individual "resonance" frequency based on MMW-evoked "sensations" of the patient (the method is called "microwave resonance therapy"). In our opinion, this procedure should be regarded as a variety of acupuncture techniques, along with electropuncture, acupressure, etc. Assuming the therapeutic efficacy of these techniques, it is no surprise that MMW can be effective as well: irradiation at about 10 mW/cm2 can also stimulate acupuncture points by subtle heating or thermal "micromassage". Clinical effects of the "MMW-puncture" are nonspecific, meaning that they are similar to those of traditional puncture-based techniques. These effects are determined by the selection of acupuncture points, intensity and duration of their stimulation, rather than by using MMW or other means for the stimulation. Therefore, studies employing the MMW-puncture seem to be of greater interest for the acupuncture practice than for the bioelectromagnetic science; such studies will be left beyond the scope of the present review.

Other areas of MMW exposure include sternum and xiphoid process, skin projection of the diseased organ, large joints, and the surface of wounds and ulcers. Once again, we could not identify the studies that originally provided the rationale and experimental proof for MMW exposure of these particular body areas. Except for the surface lesions, the radiation is unable to penetrate to diseased organs. This fact is understood and discussed by many physicians, but no proven explanation of the MMW therapy has been given yet.

Many clinical studies do not conform to conventional quality criteria (double-blind protocol, placebo treatment, adequate statistics, etc.), but still others do, and a lot of matching results has been provided by independent groups of investigators. Some clinical data on the MMW efficacy are quite impressive, and a few examples are given below (see a specialized review by Rojavin and Ziskin [1998] for additional detail).

3.5.2 Examples of MMW therapy. Korpan and Saradeth [1995] performed a double-blind controlled trial of MMW therapy for postoperative septic wounds. The study group consisted of 141 patients, 31-83 yr old, with purulent wounds after an abdominal surgery. The wounds were infected mostly with *Staphylococcus aureus* and *Bacteriodes fragiles*. MMW therapy with 1-mW/cm2, 37-GHz CW radiation was employed in 71 patients. Wound surface and adjacent soft tissue were exposed for 30 min/day for 7 days. The remaining 70 patients received placebo therapy from a similar but defective MMW generator (neither patients nor physicians knew it was defective). Radical surgical cleaning of the wounds was performed regularly in both groups. The MMW-treated patients showed 1.8 times more rapid wound clearance (5.6± 0.6 versus 10.2± 0.5 days in controls), 1.7 times earlier onset of wound granulation (4.9± 0.2 versus 8.7± 0.4 days), and 1.8 times earlier onset of epithelization (7.0± 0.4 versus 12.8± 0.6 days). The average daily decrease of wound surface area in the treated patients was twice that of the controls (7.1% versus 3.2%). The authors concluded that low intensity MMW appears to be an effective postoperative wound treatment.

Poslavsky et al. [1989] employed MMW as a monotherapy in 317 patients with duodenal and gastric ulcers. The ulcer diameter ranged from 0.3 to 3.5 cm, and the disease duration was from several months to more than 10 years. The epigastric area was exposed at 10 mW/cm2, 5.6-mm wavelength for 30 min daily, excluding weekends, until complete ulcer cicatrization. A comparable control group of 50 patients received conventional drug therapy. The ulcers cicatrized in 95.3% of MMW-treated patients, with mean healing duration of 19.8 ± 0.45 days. The respective control group values were substantially worse, namely 78% and 33.6 ± 1.12 days. The ulcer relapse rate was significantly lower after the MMW therapy.

Megdiatov et al. [1995] evaluated the efficacy of MMW therapy (42.2 GHz, 10 mW/cm2) in 52 patients with neuralgia. The radiation was applied to areas where branches of the affected trigeminal nerve approach the skin (10 exposures or sham exposures, 15 min each, concurrently with medicinal therapy). Evident clinical improvement (decrease of the incidence and severity of pain attacks) was achieved in 19 out of 27 patients treated with MMW, and only in 4 out of 25 patients receiving placebo exposures.

Liusov et al. [1995] studied MMW therapy effects in 100 patients with unstable angina pectoris (this is an intermediate condition between stable angina pectoris and infarction, and is characterized by a high risk of myocardial necrosis). The patients were divided into 4 groups. Group 1 was treated by MMW only (10 exposures of the right shoulder joint for 30 min/day, 7.1 mm); these patients ceased taking any vasodilators and antianginal medicines. In group 2, the same MMW therapy was combined with drugs (beta-adrenergic antagonists, calcium blockers, organic nitrates, etc.). Group 3 received the same drug therapy and placebo exposures, and group 4 received the drug therapy only. The therapy in groups 1 and 2 substantially decreased the rate and severity of angina attacks, making it possible to reduce the amount of nitroglycerin taken. It also decreased blood levels of malonic dialdehyde and dienic conjugates, normalized T-helper and T-suppresser ratio, reduced the diameter of venules, and increased the diameter of arterioles. No significant improvement of the lipid peroxidation system, immune status, or microcirculation was achieved in groups 3 and 4.

Karlov and co-authors [1991] used MMW in a combined therapy for cerebral circulatory disorders. The 79 patients in the study were mostly 50-80 year old and suffered from hypertensive disease and/or atherosclerosis; 61 patients were hospitalized for acute ischemic cerebral infarction, 13 for a transient disorder of the cerebral circulation, and 5 for circulatory encephalopathy. Patients were divided into two comparable groups. Both groups received the same drug therapy (hypotensive, anticoagulant, cardiotonic, and other remedies), while only the first one was also treated with MMW (10 days, 30 min/day, 4.9 mm wavelength). Patients of the second group were sham-exposed under a double-blind protocol. A favorable therapeutic effect was reported in 70% of the patients in group 1 and in 40% in group 2. MMW procedures helped decrease blood pressure, normalize the blood glucose level, and eliminate serum fibrinogen B.

The efficacy of the MMW therapy is often illustrated by individual clinical cases. Naumcheva [1994] described the history of a 54-year old male patient, who had two myocardial infarctions within a 2-year interval. He experienced severe attacks of angina both on exertion and at rest and took up to 80 nitroglycerin tablets a day (0.4 mg). Repeated courses of in- and outpatient treatment with beta-adrenoblockers, nitrates, plasmapheresis, etc. had little effect. Finally, he was hospitalized in a grave condition with a third infarction. Conventional methods were ineffective, so MMW therapy was ordered on day 10 after admission (7.1 mm wavelength, for 30 min/day to the left border of sternum). Cardialgia decreased after two exposures and nighttime pain attacks ceased after seven procedures.

The nitroglycerin intake was decreased to 1-2 tablets/day after 12 exposures. After the MMW course, the patient did not have angina attacks for 3-4 days, was able to walk up to 5 km a day, and was discharged in a satisfactory condition. Another man, age 62, was admitted to hospital with a severe macrofocal infarction, collapse, extrasystolia, and acute insufficiency and aneurysm of the left ventricle. Three days of intensive treatment still left the patient in this critical condition. Even the first MMW irradiation of sternum (5.6 mm wavelength, three 10-min exposures with 5-min intervals) had a striking effect: it arrested angina attacks and normalized sleep, and indices of hemodynamics stabilized within 5 days of the MMW therapy. The patient was discharged in a satisfactory condition and later underwent two additional MMW courses as a preventive measure.

3.5.3 Side effects of MMW therapy. As a rule, MMW therapy is well tolerated by patients, and this is regarded as one of its advantages over a drug therapy. Though most investigators reported no negative reactions to MMW, others observed them in up to 26% of patients [Golovacheva, 1995]. The possibility of induction of adverse health effects by a local, low-intensity MMW irradiation is of potential significance for setting health and safety standards and requires special attention.

Kuz'menko [1989] summarized experience with MMW use in 200 patients with cerebrovascular diseases, such as cerebral circulation insufficiency, discirculatory encephalopathy, and cerebral insult consequences. Irradiation of the sinocarotid zone at various frequencies between 58 and 62 GHz, 0.3-1 mW/cm2, was performed for 20 min/day or less, for 4 to 10 days. MMW therapy facilitated recovery in 56-77% of patients with different pathologies. However, it also caused adverse side effects, including elevation of the blood pressure (9 cases), induction of a diencephalic crisis or paroxysm during irradiation (7 cases), angina attacks (3 cases), fever (5 cases), and enhancement of menstrual bleeding (6 cases). In hypertension patients, MMW usually decreased blood pressure by 10-15 mm Hg, but occasionally increased it by 20-30 mm Hg. The author concluded that MMW can be successfully used in cerebrovascular therapy, but possible complications must be taken into account.

Afanas'eva and Golovacheva [1997] employed MMW therapy in 124 patients with stage II essential hypertension (5.6 or 7.1 mm wavelength, CW, 10 mW/cm2, 10 procedures for 30 min each). Unfavorable autonomous nervous system reactions (whole-body shivering, sweating, heart pains along with skin paling or reddening) were observed in 18 patients (15.5%). In two cases, these reactions developed into hypertensive crises, which had to be arrested by drug injections. In 33 patients (26.6%), MMW induced fluctuations of the arterial blood pressure and enhanced headaches. A temporary improvement after 4-5 exposures was followed by an increase in both systolic (by 25 ± 7.0 mm Hg) and diastolic (by 10.0 ± 2.0 mm Hg) blood pressure, which required medicinal correction. General adverse reactions after the entire MMW course (six patients; 4.8%) included sleeplessness or sleep with distressful dreams, weakness, emotional instability, and irritability. These manifestations were not profound and disappeared without further treatment. The authors emphasized that these adverse reactions were not encountered in patients who received placebo exposures.

Gun'ko and Kozshina [1993] tried MMW therapy in 528 patients with various diseases (ulcerative disease, ischemic heart disease, essential hypertension, bronchitis, pneumonia, and others). Exposures at 5.6 or 7.1 mm wavelength lasted from 15 to 60 min/day, from 5 to 18 days. Three patients, being treated for rheumatic polyarthritis, psoriasis, and duodenal ulcer (without any concurrent drug therapy), developed urticaria (hives) on the 5th-7th day of exposures. An itchy rash appeared first in the abdominal and thoracic areas,

and soon spread everywhere. Nevertheless, the treatment of the main disease in all these cases was successful. The rash disappeared 2-10 days after the completion of the MMW therapy but reappeared during the repeated MMW courses. The authors called for more studies of MMW effects on the immune system.

DISCUSSION

In this review, we have found that recent research in the MMW area covers a variety of subjects. Profound MMW effects were established at all biological levels, from cell-free systems, through cells, organs, and tissues, to animal and human organisms. While trying to avoid a general discussion of thermal versus non-thermal mechanisms in this review, we nonetheless must note that many of the reported effects were principally different from those caused by heating, and their dose and frequency dependencies often suggested nonthermal mechanisms. Regardless of the primary mechanism, the possibility of significant bioeffects of a short-term MMW irradiation at intensities at or below current safety standards deserves consideration and further study.

The major question about FSU publications in the MMW area is their reliability. A number of studies cited here were performed at the highest scientific level. Other studies, perhaps the majority of those cited, were flawed, but may still bear valuable information and should not be discarded without proper analysis.

For example, free-field dosimetry in the MMW band is a serious technical problem. As of our knowledge, no commercially available probes, even in the U.S., are rated for near-field measurements in the MMW band. Therefore, it is not surprising that many investigators, particularly clinicians, have had to rely on manufacturer-specified field intensities, such as 10 mW/cm2 for "Yav'-1" therapeutic generator. One may doubt if the field actually was 5, 10, or 15 mW/cm2, but under no circumstances could it exceed a spatial average of, say, 50 mW/cm2, which is beyond the generator's capabilities. Thus, while the precise exposure parameters may not be known, a range of possible exposure intensities may be estimated. With understanding of this fact, the experimental data may still be important and usable.

Another widespread shortcoming of clinical studies is that MMW therapy is compared to drug therapy, without using a sham-exposed control group. MMW therapy was often reported to be more effective than drugs, which could be a placebo effect; but if this were the case, one would have to conclude that placebo was more effective than modern drug therapy. This possibility could certainly be true for certain patients and certain disorders, but does not seem feasible for large populations and a wide scale of diseases.

A further source of skepticism about findings made by FSU scientists is that they have not been replicated in the West. Replication is much needed indeed, but it can hardly be anticipated without adequate attempts. To our knowledge, only three laboratories throughout the US (less than 10 scientists total) are currently doing any research on MMW bioeffects, which is by no means sufficient to match the amount and variety of the FSU research. Besides, many cited studies are very recent (1995-1997), so replication has yet to be expected.

With all the diversity of the MMW research, and differences in studied subjects and endpoints, some particulars appear to be common for various situations and MMW effects. Considering these particulars may be critical for replication studies:

1. Individuals or groups in a population, which would usually be regarded as uniform, may react to MMW in rather different or even opposite ways. For example, Temur'iants et al. [1993, 1994] divided the vivarium population of rats by their open-field activity before performing exposures. Not only reactions to MMW, but also reactions to immobilization stress, were very different in animals with low, medium, and high activity levels. Pooling all the data together, as well as neglecting the intrinsic differences in the population, would have inevitably masked MMW effects.

2. There seem to exist unknown and uncontrolled factors that determine the MMW sensitivity of a specimen or a population. Irradiation could increase antibiotic resistivity in one experiment and decrease it in the next one [Bulgakova et al., 1996]; it increased the beating rate in one isolated heart and decreased it in the other [Chernyakov et al., 1989]; MMW-therapy usually decreased blood pressure, but eventually increased it greatly [Kuz'menko, 1989]. As long as these changes exceeded the "noise" level and were not produced by a sham exposure, they can be regarded as MMW effects. Again, pooling all data together, regardless of the direction of changes, could easily mask an MMW effect.

3. Even robust MMW effects may be well reproducible for a limited time and then disappear. The effects of complete suppression or 200-400% enhancement of chloride transmembrane current in alga cells were far beyond any spontaneous variations and could hardly be confused with any artifact [Kataev et al., 1993]. However, both effects weakened and disappeared by the end of winter without any apparent reason. MMW effects on isolated frog nerve also disappeared in spring [Burachas and Mascoliunas, 1989], suggesting that MMW sensitivity may be somehow related to the base level of metabolism.

4. MMW effects could often be revealed only in subjects with already some deviation from the "normal" state. MMW caused little or no reactions in intact animals, but significantly alleviated effects of immobilization, ionizing radiation, etc. Many clinical studies claim that MMW therapy is effective only when one or another kind of pathology is present, while in a healthy organism MMW will not produce any reactions (however, this thesis has not been adequately proven).

5. Increased sensitivity and even hypersensitivity of individual specimens to MMW may be real. Depending on the exposure characteristics, especially wavelength, a low-intensity MMW radiation was perceived by 30 to 80% of healthy examinees [Lebedeva, 1993, 1995]. Some clinical studies reported MMW hypersensitivity, which was or was not limited to a certain wavelength [Golovacheva, 1995]. In a study by Afanas'eva and Golovacheva [1997], adverse health reactions to MMW appeared only in women (100%), only with a labile course of angina pectoris (100%), and most of them were in the menopausal period (66.7%). The authors suggested that this category of people is particularly sensitive to MMW.

It is important to note that, even with the variety of bioeffects reported, no studies have provided evidence that a low-intensity MMW radiation represents a health hazard for human beings. Actually, none of the reviewed studies with low-intensity MMW even pursued the evaluation of health risks, though in view of numerous bioeffects and growing usage of MMW technologies this research objective appears very reasonable. Such MMW effects as alterations of cell growth rate and UV light sensitivity, biochemical and antibiotic resistivity changes in pathogenic bacteria, as well as many others are of potential significance for safety standards. MMW therapy in many cases employs field intensities comparable to or lower than allowed by current safety standards; still, even local and short-term exposures were reported to produce marked effects. It should also be realized that biological effects of a prolonged or chronic MMW exposure of the whole body or a large body area have never

been investigated. Safety limits for these types of exposure are based solely on predictions of energy deposition and MMW heating, but in view of recent studies this approach is not necessarily adequate.

The significance of MMW bioeffects for human health, considering both safety limitations and possible clinical applications, should be neither over- nor underestimated. It is, however, an intriguing and potentially important area that needs to be further explored. If this present review draws attention to the MMW research and stimulates new studies, we will consider its goal accomplished.

ACKNOWLEDGEMENTS

The work was supported in part by the U.S. Army Medical Research and Materiel Command and the U.S. Air Force Armstrong Laboratory under US Army contract DAMD17-94-C-4069 awarded to McKesson BioServices. The views expressed in this article are those of the authors and should not be construed as reflecting the official policy or position of the Department of the Army, Department of the Air Force, Department of Defense, or the United States Government.

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Footnotes

1 EMF Database is produced by Information Ventures, Inc. (Philadelphia, PA) and covers topics related to biological effects of electromagnetic fields, from DC to submillimeter wavelengths. The Database contains over 20,000 citations of relevant publications from various sources, including peer-reviewed journals, books, proceedings, and meeting abstracts. Available citations are assimilated in the Database without any pre-selection based on the language, affiliation of the authors, or relevance to a particular EMF frequency range.

TABLE 1. Other in vitro effects of millimeter wave radiation

Citation	Endpoints / Findings	Exposure conditions	Details
1	2	3	4
Berzhanskaya et al., 1995	Suppression of bioluminescence of *Photobacterium leiognathi*	36.2 to 55.9 GHz 1.3 to 48.0 m W/cm^2 MMW heating < 0.1 ^{o}C	The effect reached maximum within 10 min, with a gradual recovery after the cessation of exposure, and could be repeated many times in the same cell culture. The maximum effect (16-18% decrease) was caused by the lower frequencies. At 36.2 GHz, 1.3 and 13 m W/cm2 intensities produced virtually the same effect.
Mudrick et al., 1995	Changes in the intensity of $BaSO_4$-induced flash of chemoluminescence in the presence of luminol in human leukocytes	42.19, 46.84, or 53.53 GHz 1 mW/cm^2 30 min	The effect depended on the frequency, and the dependence was individual for blood samples from each particular donor. The maximum observed effect was a twofold flash enhancement ($p<0.01$) at 42.19 GHz.
Gapeev et al., 1996	Inhibition of the luminol-dependent chemoluminescence of neutrophils activated by opsonized zymosan	41.8 to 42.05 GHz 0.15-0.25 mW/cm^2	In the near zone of the irradiator, the effect depended on the radiation frequency in a quasi-resonance manner, while in the far field it was independent of the frequency.
Logani and Ziskin, 1996	No MMW effect on lipid peroxidation in phosphatidylcholine liposomes	53.6, 61.2, or 78.2 GHz 10, 1, and 500 mW/cm^2, respectively, 30 or 60 min	MMW did not increase the level of lipid peroxidation under any of the experimental conditions (in liposomes loaded or not loaded with melanin, or in the presence or absence of iron (III) adenosine diphosphate).

TABLE 1. *(continued)*

1	2	3	4
Roshchupkin et al., 1994, 1996	MMW changed aggregation of thymocytes with erythrocytes in a dose- and frequency-dependent manner	46.12 or 46.19 GHz either: *(1)* at 0.35 mW/cm2, 0 to 120 min, or: *(2)* 0.05 to 0.5 mW/cm2, 90 min	*(1)* The threshold was 60 min for both frequencies, increasing the number of aggregates to 115-140% of the parallel control. The effect of 46.12 GHz did not change when the exposure duration was further increased to 90 or 120 min, while the effect of 46.19 GHz fell to 80-90%. *(2)* The threshold was 0.25-0.35 mW/cm2. The effect of 46.19 GHz stayed at 110-120% at 0.35 and 0.5 mW/cm2, while the effect of 46.12 GHz grew linearly to 170% at 0.5 mW/cm2
Shub et al., 1995	Changes in transmissivity of R-plasmids in various strains of *E. coli* and *S. aureus*	6.0-6.7 mm band, < 1 mW/cm^2 30 min	A number of biologically-active frequencies affected the transmissivity of R-plasmids, either decreasing or increasing plasmid- and chromosome-dependent resistivity to antibiotics Irradiation for 60 min had a bacteriostatic effect, which was not related to the activity of the recA-dependent DNA repair. Cells carrying Ia , Ij, N, and E plasmids appeared to be protected from the antibacterial effect of MMW.
Kazbekov and Vyacheslavov, 1987	No nonthermal effects in prototrophic, thymidine-deficient, and tryptophan-requiring strains of *E. coli* and *B. subtilis*	6- to 7.8-mm wavelengths 5 mW/cm^2	MMW either had no effect on studied parameters (thymine and thymidine uptake, potassium leakage, hydrogen ion release, uptake of DNA, etc.), or produced the same changes as conventional heating by 1-2 ^{o}C.

Figure 1. Absolute numbers and percentages of publications on topics related to biological action of millimeter waves versus years of publication.

The graph is based on counts of citations in the EMF Database v. 3.0, 1997. Studies by the former Soviet Union (FSU) scientists and by all others (non-FSU) were counted separately. Vertical scale is the number of published MMW studies per 2-year time intervals (abscissa). Numbers next to the datapoints indicate the weight (%) of MMW studies in the FSU and non-FSU bioelectromagnetic research (i.e., the percentage of MMW studies relative to the total number of studies included in the EMF database for the respective time periods)

Source http://www.rife.org/otherresearch/millimeterwaves.html