SECTION 15

Evidence for Disruption by Modulation Role of Physical and Biological Variables in Bioeffects of Non-Thermal Microwaves for Reproducibility, Cancer Risk and Safety Standards

2012 Supplement

Prof. Igor Belyaev, Ph D, Dr Sc

Associate Professor, Faculty of Natural Sciences

Stockholm University, Stockholm, Sweden

Head Research Scientist, Laboratory of Molecular Genetics, Cancer Research Institute

Slovak Academy of Science, Bratislava, Slovakia

Head Research Scientist, Laboratory of Radiobiology

General Physics Institute, Russian Academy of Science

Moscow, Russia

Prepared for the BioInitiative Working Group
September 2012

ABSTRACT

Diverse biological responses to non-thermal (NT) microwaves (MW), including adverse health effects related to increased cancer risk, have been studied by multiple research groups all over the world. In approximately half of these studies, no any effects were found (negative studies), while the other half reported the NT MW effects (positive studies). This fact is often referred to as non-reproducibility of the NT MW effects. In most cases, such a conclusion is based on comparing studies, which significantly differ in important biological and physical variables/parameters. The aim of this chapter is to provide an overview of the complex dependence of the NT MW effects on various physical and biological parameters, which must be controlled in replication studies. To the aim of this paper, all studies available to the author, which included analysis of different variables/parameters and reported some positive NT MW response to be a reference for analyzing its dependence on physical and biological parameters, were included. Selection criteria included relevant experimental design, methodological quality and statistical analysis. Besides dependencies on carrier frequency, modulation, genotype, physiological traits, presence of radical scavengers and antioxidants, reported by many research groups, the emerging data suggest dependencies of the NT MW effects on polarization, intermittence and coherence time of exposure, static magnetic field, electromagnetic stray fields, sex, age, individual traits, cell density during exposure. This overview provides clear evidence that in most cases, the references to non-reproducibility of the NT MW effects are not correct. Unfortunately, most reviews and panels in the field do not include analysis of various biological variables and physical parameters when comparing the data on the NT MW effects from different studies. As result, misleading conclusion is often made that MW at NT levels produce no “reproducible” effects. Our analysis suggests that different (bandwidth, frequency, modulation, polarization) NT MW signals should be considered as separate agents in setting the safety standards. The data also indicate that duration of exposure may be as important as power density (PD) and specific absorption rate (SAR), and, therefore, the "dose" and duration of exposure should also be considered in safety standards along with PD/SAR. Further evaluation of the dependencies of NT MW effects on biological and physical variables/parameters are needed for understanding the mechanisms by which NT MW affect biological systems, planning *in vivo* and epidemiological studies, setting the safety standards, and minimizing the adverse effects of MW from mobile communication.

Keywords: non-thermal effects of microwaves, mobile (cellular) phones, safety standards.

List of Abbreviations:

Anomalous viscosity time dependence (AVTD); blood-brain barrier (BBB); catalase (CAT); Digital Enhanced (former European) Cordless Telecommunications (DECT); circularly polarized (CP); continuous wave (CW); Digital Advanced Mobile Phone System (DAMPS); discontinuous transmission (DTX); electroencephalographic (EEG); electromagnetic field (EMF); embryonic stem (ES) cells; ethidium bromide (EtBr); extremely low frequency (ELF); Gaussian Minimum Shift Keying (GMSK); Ginkgo biloba (Gb); Global System for Mobile Communication (GSM); glutathione peroxidase (GSH-Px); International Commission for Non-Ionizing Radiation Protection (ICNIRP); linearly polarized (LP); malondialdehyde (MDA); micronucleus (MN) assay; microwaves (MWs); N-acetyl-beta-d-glucosaminidase (NAG); nitric oxide (NO); non-thermal (NT); ornithine decarboxylase (ODC); phorbol ester 12-myristate 13-acetate (PMA); phosphorylated H2AX histone (γ-H2AX); power density (PD); regional cerebral blood flow (rCBF); Russian National Committee on Non-Ionizing Radiation Protection (RNCNIRP); specific absorption rate (SAR); static magnetic field (SMF); superoxide dismutase (SOD); Time Division Multiple Access (TDMA); tumor suppressor p53 binding protein 1 (53BP1); ultraviolet (UV); Universal Mobile Telecommunications System (UMTS).

I. THERMAL VERSUS NON-THERMAL EFFECTS

Exposures to electromagnetic fields vary in many parameters: power (specific absorption rate, incident power density), wavelength/frequency, near field/far field, polarization (linear, circular), continues wave (CW) and pulsed fields (that include variables such as pulse repetition rate, pulse width or duty cycle, pulse shape, pulse to average power, etc.), modulation (amplitude, frequency, phase, complex), static magnetic field (SMF) and electromagnetic stray fields at the place of exposure, overall duration and intermittence of exposure (continuous, interrupted), acute and chronic exposures. With increased absorption of energy, so-called thermal effects of microwaves (MW) are usually observed that deal with MW-induced heating. Specific absorption rate (SAR) or power density (PD) is a main determinate for thermal MW effects. Several other physical parameters of exposure have been reported to be of importance for so-called non-thermal (NT) biological effects, which are induced by MW at intensities well below any measurable heating (Grundler, Jentzsch et al. 1988; Iskin 1990; Devyatkov, Golant et al. 1994; Pakhomov, Akyel et al. 1998; Adey 1999; Belyaev, Shcheglov et al. 2000; Betskii, Devyatkov et al. 2000; Banik, Bandyopadhyay et al. 2003; Grigoriev, Stepanov et al. 2003; Grigoriev 2004; Lai 2005; Belyaev 2010; Cifra, Fields et al. 2011) (Pakhomov and Murphy 2000).

Most often, current safety standards are based on thermal MW effects observed in short-term (acute) exposures. On the other hand, NT MW effects, especially those induced during prolonged (chronic) exposures, are accepted and taken into account for setting the national safety standards in some countries such as Russia (Grigoriev, Stepanov et al. 2003; Grigoriev 2004; Grigoriev, Nikitina et al. 2005). It should be noted that, in contrast to the ICNIRP (International Commission for Non-Ionizing Radiation Protection) safety standards (ICNIRP 1998) which are based on the acute thermal effects of MW, the standards adopted by the Russian National Committee on Non-Ionizing Radiation Protection (RNCNIRP) are based on experimental data from chronic (up to 4 month) exposures of animals to MW at various physical parameters including intensity, frequency and modulation, obtained from research performed in the former Soviet Union (Grigoriev, Stepanov et al. 2003; Grigoriev 2004; Grigoriev, Nikitina et al. 2005).

Since setting the current safety standards, the situation with exposure of the general population to MW has changed significantly. Nowadays, most of the human population is chronically exposed to MW signals from various sources including mobile phones and base stations. These exposures are characterized by low intensities, varieties and complexities of signals, and long-term durations of exposure that are comparable with a lifespan. So far, the “dose” (accumulated absorbed energy that is measured in radiobiology as the dose rate multiplied by exposure time) is not adopted for the MW exposures and SAR or PD is usually used for guidelines. To what degree SAR/PD can be applied to the nowadays NT MW chronic exposures is not known and the current state of research demands reevaluation of the safety standards (Grigoriev, Nikitina et al. 2005).

The literature on the NT MW effects is very broad. About half of available experimental studies report non-thermal biological effects of microwaves (Huss, Egger et al. 2007). There are four lines of evidence for the NT MW effects: (1) altered cellular responses in laboratory *in vitro* studies and results of chronic exposures *in vivo* studies (Grigoriev, Stepanov et al. 2003; Lai 2005; Cook, Saucier et al. 2006); (2) results of medical application of NT MW in the former Soviet Union countries (Sit'ko 1989; Devyatkov, Golant et al. 1994; Betskii, Devyatkov et al. 2000; Pakhomov and Murphy 2000; Pakhomov and Murphy 2000); (3) hypersensitivity to electromagnetic fields (EMF) ; (4) epidemiological studies suggesting increased cancer risks from using mobile phones longer than 10 years (Kundi, Mild et al. 2004; Lonn, Ahlbom et al. 2004; Hardell, Eriksson et al. 2005).

The first data on the NT effects of MW in so-called millimeter range (wavelength 1-10 mm in vacuum) was obtained by Vilenskaya and co-authors (Vilenskaya, Smolyanskaya et al. 1972) and Devyatkov (Devyatkov 1973). Highly resonant effects of ultra-weak MW (near 70 GHz) on the

induction of λ-phage were first established by Webb (Webb 1979), and subsequently corroborated (Lukashevsky and Belyaev 1990). In these and subsequent studies the observed spectra of MW action were found to have the following common properties: (*1*) the MW effects were strongly dependent on the frequency (frequency windows), (*2*) there was an associated power (intensity) threshold below which no effect was observed, and above which the effects of exposure depended only weakly on power over several orders of magnitude (so-called S-shaped or sigmoid dependence), (*3*) the occurrence of MW effects depended on the duration of exposure, a certain minimum duration of exposure was necessary for an effect to manifest itself. These important regularities of the NT MW effects have previously been reviewed (Postow and Swicord 1986; Grundler, Jentzsch et al. 1988; Golant 1989; Iskin 1990; Belyaev 1992; Devyatkov, Golant et al. 1994; Pakhomov, Akyel et al. 1998; Hyland 2000; Pakhomov and Murphy 2000).

The first investigations of the NT MW effects at lower frequency ranges were performed by several research groups in USSR (Presman, IuI et al. 1961; Presman 1963) and in USA by Frey (Frey 1967; Frey 1974), Blackman and colleagues (Blackman, Benane et al. 1980; Blackman, Benane et al. 1980; Joines and Blackman 1980) and Adey and colleagues (Adey, Bawin et al. 1982; Lin-Liu and Adey 1982). These groups found dependence of the NT MW effects on modulation. The effect of pulse-modulated MW was related to peak power, whereas average power was found to be relatively unimportant (Frey 1974). Frequency dependence of the MW effects have been reported (Frey 1974).

Since that time, other groups have confirmed and extended the main findings of these pioneering studies. Below, survey of recent studies, which evaluate dependence of the NT MW effects on physical parameters and biological variables, is provided.

II. FREQUENCY DEPENDENCE AND FREQUENCY WINDOWS

The effects of NT MW on DNA repair in *E. coli* K12 AB1157 were studied by the method of anomalous viscosity time dependence (AVTD) (Belyaev, Alipov et al. 1992; Belyaev, Alipov et al. 1992). The AVTD method is a sensitive technique to detect changes in conformation of nucleoids/chromatin induced by either genotoxic or stress factors (Belyaev and Harms-Ringdahl 1996; Belyaev, Shcheglov et al. 1996; Belyaev, Alipov et al. 1997; Sarimov, Malmgren et al. 2004; Belyaev, Hillert et al. 2005; Markova, Hillert et al. 2005). Significant inhibition of DNA repair was found when X-ray-irradiated cells were exposed to MW within the frequency ranges of 51.62-51.84 GHz and 41.25-41.50 GHz. The effects were observed within two “frequency windows”, both

displaying a pronounced resonance character with the resonance frequencies of 51.755 GHz and 41.32 GHz, respectively (Belyaev, Alipov et al. 1992; Belyaev, Alipov et al. 1992). Of note, these MW effects were observed at PD well below any thermal effects and could not be accounted for by heating. The frequency windows of resonance type have often been termed "resonances" as also will be used below.

The resonance frequency of 51.755 GHz was stable within the error of measurements, $\pm$1 MHz with decreasing the PD from $3 \cdot 10^{-3}$ to 10^{-19} W/cm^2 (Belyaev, Alipov et al. 1992; Belyaev, Shcheglov et al. 1996). At the same time, the half-width of the resonance decreased from 100 MHz to 3 MHz revealing an extremely sharp dependence on frequency ($Q \sim 10^4$). This sharp narrowing of the 51.755 GHz resonance with decreasing the PD from $3 \cdot 10^{-3}$ to 10^{-7} W/cm^2 followed by an emergence of new resonances, 51.675$\pm$0.001, 51.805$\pm$0.002, and 51.835$\pm$0.005 GHz (Belyaev, Shcheglov et al. 1996; Shcheglov, Belyaev et al. 1997). The half-widths of all these resonances including the main one, 51.755$\pm$0.001 GHz, were about 10 MHz at the PD of 10^{-10} W/cm^2. These data were interpreted in the framework of the model of electron-conformational interactions as a splitting of the main resonance 51.755 GHz by the MW field (Belyaev, Shcheglov et al. 1996).

The MW effects were studied at different PD and several frequencies around the resonance frequency of 51.675 GHz (Shcheglov, Belyaev et al. 1997). This resonance frequency was found to be stable, $\pm$1 MHz, within the PD range of 10^{-18} - 10^{-8} W/cm^2. Along with disappearance of the 51.675 GHz resonance response at the sub-thermal PD of 10^{-6} - 10^{-3} W/cm^2, a new resonance effect arose at 51.688$\pm$0.002 GHz (Shcheglov, Belyaev et al. 1997). This resonance frequency was also stable within the PD range studied.

Taken together, the data on NT MW effects on chromatin (Belyaev, Alipov et al. 1992; Belyaev, Shcheglov et al. 1996; Shcheglov, Belyaev et al. 1997) suggested a sharp rearrangement of the frequency spectra of MW action, which was induced by the sub-thermal MW (Belyaev, Alipov et al. 1992; Belyaev, Shcheglov et al. 1996; Shcheglov, Belyaev et al. 1997). The half-widths of all three resonances depended on PD, changing either from 2-3 MHz to 16-17 MHz (51.675 GHz and 51.668 GHz resonances) or from 2-3 MHz to 100 MHz (51.755 GHz resonance) (Belyaev, Shcheglov et al. 1996; Shcheglov, Belyaev et al. 1997). The data indicated also that dependencies of half-width on PD might vary for different resonance frequencies.

Significant narrowing in resonance response with decreasing PD has been found when studying the growth rate in yeast cells (Grundler 1992) and chromatin conformation in thymocytes of rats (Belyaev and Kravchenko 1994). In the Gründler's study, the half-width of the resonance (near 41 GHz) decreased from 16 MHz to 4 MHz as PD decreased from 10^{-2} W/cm^2 to 5 pW/cm^2 (Grundler 1992).

Thus, the results of studies with different cell types indicate that narrowing of the resonance window upon decrease in PD is one of the general regularities in cell response to NT MW. This regularity suggests that many coupled oscillators are involved non-linearly in the response of living cells to NT MW as has previously been predicted by Fröhlich (Frohlich 1968).

Gapeev et al. studied effects of MW exposure (frequency range 41.75-42.1 GHz, frequency increment 50 MHz, PD 240 $\mu W/cm^2$) on the respiratory burst induced by calcium ionophore A23187 and phorbol ester 12-myristate 13-acetate (PMA) in the peritoneal neutrophils of mice (Gapeev, Safronova et al. 1996; Gapeyev, Safronova et al. 1997). MW inhibited the respiratory burst. MW effect displayed resonance-like dependence on frequency, the resonance frequency and half-width of the resonance being 41.95 GHz and 160 MHz, respectively (Q= 260) (Gapeev, Safronova et al. 1996; Gapeyev, Safronova et al. 1997). In other studies, Gapeev et al. analyzed acute zymosan-induced paw edema in mice (Gapeyev, Mikhailik et al. 2008; Gapeyev, Mikhailik et al. 2009). MW exposure of animals at the PD of 0.1 mW/cm^2 resulted in decrease of the paw edema that was frequency-dependent in the range of 42-43 GHz.

Based on the extrapolation from the data obtained in the extremely high frequency range (30-300 GHz), the values for half-width of resonances at the frequency range of mobile phones (0.9–2 GHz) were estimated to be 1-10 MHz (Sarimov, Malmgren et al. 2004). Effects of GSM (Global System for Mobile Communication) MW on chromatin conformation and 53BP1 (tumor suppressor p53 binding protein 1)/γ-H2AX (phosphorylated H2AX histone) DNA repair foci in human lymphocytes were studied in this frequency range (Sarimov, Malmgren et al. 2004; Belyaev, Hillert et al. 2005; Markova, Hillert et al. 2005; Belyaev, Markova et al. 2009). These MW effects depended on carrier frequency (Sarimov, Malmgren et al. 2004; Markova, Hillert et al. 2005; Belyaev, Markova et al. 2009). This dependence was replicated in independent experiments with lymphocytes from twenty six healthy and hypersensitive persons (Belyaev, Hillert et al. 2005; Markova, Hillert et al. 2005; Belyaev, Markova et al. 2009).

Tkalec and colleagues exposed duckweed (*Lemna minor L.*) to MW at the frequencies of 400, 900, and 1900 MHz (Tkalec, Malaric et al. 2005). The growth of plants exposed for 2 h to a 23 V/m electric field of 900 MHz significantly decreased in comparison with the control, while an electric field of the same strength but at 400 MHz did not have such effect. A modulated field at 900 MHz strongly inhibited the growth, while at 400 MHz modulation did not influence the growth significantly. At both frequencies, a longer exposure mostly decreased the growth and the highest electric field (390 V/m) strongly inhibited the growth. Exposure of plants to lower field strength (10 V/m) for 14 h caused a significant decrease at 400 and 1900 MHz while 900 MHz did not influence the growth. Peroxidase activity in exposed plants varied, depending on the exposure characteristics.

Observed changes were mostly small, except in plants exposed for 2 h to 41 V/m at 900 MHz where a significant increase (41%) was found. The authors concluded that MW might influence plant growth and, to some extent, peroxidase activity. However, the effects of MW strongly depended on the characteristics of the field exposure such as frequency and modulation. These dependences were replicated in further studies (Tkalec, Malaric et al. 2007; Tkalec, Malaric et al. 2009).

Remondini et al. analyzed changes in gene expression in human EA.hy926 endothelial cells using gene microarrays (Remondini, Nylund et al. 2006). Cells were exposed to MW (SAR 1.8-2.5 W/kg, 1 h exposure) either at 900-MHz GSM Basic mode or 1800-MHz GSM Basic mode. Exposure to 900 MHz resulted in up-regulation in 22 genes and down-regulation in 10 genes. No significant change in gene expression was observed after exposure to 1800 MHz.

III. NON-LINEARITY: SIGMOID INTENSITY DEPENDENCES AND POWER WINDOWS

Devyatkov with colleagues have found and published in Russian that wide variety of NT MW effects *in vitro* and *in vivo* display sigmoid dependence on intensity above certain intensity thresholds (Devyatkov 1973).

In English literature, one of the earliest observation of threshold in response to NT MW was published by Frey (Frey 1967). In this study, the threshold of 30 μW/cm2 was found in the study by Frey on Brain stem evoked responses to RF in cats (Frey 1967). This value was 4 orders of magnitude lower then intensities needed to cause internal body temperature increase.

In their pioneering study on blood-brain barrier (BBB) permeability, Oscar and Hawkins exposed rats to MW at 1.3 GHz and analyzed BBB permeability by measuring uptake of several neutral polar substances in certain areas of the brain (Oscar and Hawkins 1977). A single, 20 min exposure, to continuous wave (CW) MW increased the uptake of D-mannitol at average power densities of less than 3 mW/ cm^2. Increased permeability was observed both immediately and 4 h after exposure, but not 24 h after exposure. After an initial rise at 0.01 mW/ cm^2, the permeability of cerebral vessels to saccharides decreased with increasing microwave power at 1 mW/cm^2. Thus, the effects of MW were observed within the power window of 0.01- 0.4 mW/cm^2. The findings on "power windows" for BBB permeability have been subsequently corroborated by the group of Persson and Salford (Salford, Brun et al. 1994; Persson, Salford et al. 1997). In their recent study, the effects of GSM MW on the permeability of the BBB and signs of neuronal damage in rats were investigated using a real GSM programmable mobile phone in the 900 MHz band (Eberhardt, Persson et al. 2008). The rats were exposed for 2 h at an SAR of 0.12, 1.2, 12, or 120 mW/kg.

Albumin extravazation and also its uptake into neurons increased after 14 d. The occurrence of dark neurons in the rat brains increased later, after 28 d. Both effects were seen already at 0.12 mW/kg with only slight increase, if any, at higher SAR values.

Sigmoid intensity dependences and power windows for the NT MW effects were observed in many other studies as previously reviewed (Postow and Swicord 1986; Grundler, Jentzsch et al. 1988; Golant 1989; Iskin 1990; Devyatkov, Golant et al. 1994; Blackman 2009).

Since 1980, there have been numerous reports of biological effects that show intensity "windows", that is, regions of intensity that cause changes surrounded by higher and lower intensities that show no effects from exposure, see for review (Blackman 2009). These results mean that lower intensity is not necessarily less bioactive, or less harmful.

Olcerst at al have reported that MW-induced increase in rubidium passive efflux did not increase monotonically with absorbed power (Olcerst, Belman et al. 1980). In fact, the highest exposure (SAR 390 mW/g) resulted in an increase, not statistically different from the lowest exposure level (SAR 100 mW/g) For sodium ions, at the greatest SAR of 390 mW/g, the effect was the smallest (Olcerst, Belman et al. 1980).

The data obtained in experiments with *E coli* cells and rat thymocytes provided new evidence for sigmoid type of PD dependence and suggested that, similar to ELF effects, MW effects may be observed within specific "intensity windows" (Belyaev, Shcheglov et al. 1992; Belyaev and Kravchenko 1994; Belyaev, Shcheglov et al. 1996; Shcheglov, Belyaev et al. 1997). The most striking example of the sigmoid PD dependence was found at the resonance frequency of 51.755 GHz (Belyaev, Shcheglov et al. 1996). When exposing *E. coli* cells at the cell density of $4 \cdot 10^8$ cell/ml, the effect reached saturation at the PD of 10^{-18}-10^{-17} W/cm^2 and did not change up to PD of 10^{-3} W/cm^2. In these experiments, the direct measurements of PD below 10^{-7} W/cm^2 were not available and lower PD was obtained using calibrated attenuators. Therefore, some uncertainty in the evaluation of the lowest PD was possible. The background MW radiation in this frequency range has been estimated to be 10^{-21}-10^{-19} W/m^2/Hz (Kolbun and Lobarev 1988). Based on the experimentally determined half-width of the 51.755 GHz resonance, 1 MHz (Belyaev, Shcheglov et al. 1996), the background PD was estimated as 10^{-19}-10^{-17} W/cm^2 within the 51.755 GHz resonance. The resonance MW effects on *E. coli* cells were observed at the PD very close to the estimated background value (Belyaev, Shcheglov et al. 1993; Belyaev, Alipov et al. 1994; Belyaev, Shcheglov et al. 1996; Shcheglov, Belyaev et al. 1997; Shcheglov, Alipov et al. 2002). These data suggested that the PD dependence of MW effect at the specific resonance frequencies might have intensity threshold just slightly above the background level. Dependence of the MW effect on PD at one of the resonance frequencies, 51.675 GHz, had the shape of "intensity window" in the PD range

from 10^{-18} to 10^{-8} W/cm^2 (Shcheglov, Belyaev et al. 1997). It is interesting, that no MW effect at this resonance frequency was observed at sub-thermal and thermal PD. This type of PD dependence has supported hypothesis about possible rearrangement of the frequency MW spectra action by the MW field (Belyaev, Shcheglov et al. 1996). The position of the PD window varied between different resonance frequencies and depended on cell density during exposure of cells (Shcheglov, Belyaev et al. 1997). Despite some uncertainty in the evaluation of PD at the levels below 10^{-7} W/cm^2 in the referred studies the data indicated that NT MW at the resonance frequencies may result in biological effects at very low intensities comparable with intensities from base stations and other MW sources used in mobile communication.

Gapeev et al. have studied dependence of the MW effects at the resonance frequency of 41.95 GHz on the respiratory burst induced by calcium ionophore A23187 and PMA in the peritoneal neutrophils of mice (Gapeev, Safronova et al. 1996; Gapeyev, Safronova et al. 1997). Inhibitory effects of MW exposure has been observed at the PD of 0.001 mW/cm^2 and displayed sigmoid dependence on PD at higher power densities (Gapeev, Safronova et al. 1996; Gapeyev, Safronova et al. 1997). In other study, Gapeev et al. analyzed acute zymosan-induced paw edema in mice (Gapeyev, Mikhailik et al. 2009). MW exposure of animals at the frequency of 42.2GHz and exposure duration of 20 min decreased the paw edema. Sigmoid dependence of this effect on PD has been obtained with a maximum at the PD of 0.1 mW/cm^2.

French et al. exposed human astrocytoma cells to EMR at 835 MHz at a power density of either 40 mWcm^2 or 8.1 mWcm^2 (French, Donnellan et al. 1997). Lower power signal was more potent than high power signal. At the lower power density, it was observed that the rate of DNA synthesis decreased, and that the cells flattened and spread out in comparison to unexposed cultures. At higher power density there were no effects seen on cell proliferation, but alteration in cell morphology included increased cell spreading and also the appearance of actin-containing blebs at localized sites on the membrane. It was hypothesized that 835 MHz radiation at low power density may be affecting a signal transduction pathway involved in cell proliferation.

Sigmoid dependence of the negative impact of mobile phone usage on semen quality in human males was found in recent study analyzing motility, vitality, ROS generation by the whole cell, ROS generation by the mitochondria, oxidative DNA damage and DNA fragmentation (De Iuliis, Newey et al. 2009). Specifically, all of the responses examined showed an extremely rapid change at low SAR exposures that then reached a plateau at a point where around 30% of the sperm population was affected.

Hintzsche et al. have recently reported sigmoid dependence on PD in the range up to 4.3 mW/cm^2 for non-thermal effects of MW on mitotic spindle in human-hamster hybrid cells (Hintzsche, Jastrow et al. 2011).

Sun et al. have investigated the effects of exposure to a 1.8-GHz radiofrequency radiation (RFR) at different intensities on epidermal growth factor (EGF) receptor clustering and phosphorylation in human amniotic (FL) cells (Sun, Shen et al. 2012). The results showed that exposure to RFR at specific absorption rate (SAR) of 0.5, 1.0, 2.0, or 4.0 W/kg for 15 min significantly induced EGF receptor clustering and enhanced phosphorylation of the tyrosine-1173 residue in FL cells. The RFR effect displayed a sigmoid-dependence on SAR with a prominent plateau in the range of 0.5-4 W/kg and a threshold below 0.5 W/kg.

It should be mentioned that almost all biophysical mechanisms, which have previously been proposed to account for NT MW effects, predict thresholds in dependence of these effects in intensity (Grundler, Jentzsch et al. 1988; Golant 1989; Iskin 1990; Devyatkov, Golant et al. 1994; Golo 2005; Matronchik and Belyaev 2008).

To conclude, since 1970, there have been numerous reports of biological effects that show thresholds, sigmoid dependence of the NT MW effects on intensity and also "power windows", that is, regions of intensity that cause changes surrounded by higher and lower intensities that show no effects from exposure. These results mean that: (i) lower intensity is not necessarily less bioactive, or less harmful;(ii)the NT effects may be observed at intensities above thresholds which are very close to background levels and similar to intensities from base stations.

IV. DOSE AND DURATION OF EXPOSURE

So far, the "dose" (accumulated absorbed energy that is measured in radiobiology as the dose rate multiplied by exposure time) is not adopted for the MW exposures and PD or SAR (dose rate analog in radiobiology) is usually used for guidelines. To what degree SAR/PD can be applied to the nowadays NT MW chronic exposures is not exactly known and the current state of research demands reevaluation of the safety standards (Grigoriev, Nikitina et al. 2005).

Based on mechanistic consideration of the NT MW effects, Frey has suggested that the toxicology model used by investigators was not the appropriate model on which to design MW experiments (Frey 1993). With chemical substance in a toxicology model, a dose-response relationship is usually observed: the greater the dose, the greater the effect. In analogy with toxicology, MW experiments tended to be designed with high doses and with little regard for other parameters such

as modulation and frequency. This might be one reason why many MW studies yielded so little useful information (Frey 1993).

The role of exposure duration in combination with dose rate/SAR for appearance and persistence of the NT MW effects have been analyzed by many research groups using various end-points.

Koveshnikova et al. exposed rats to pulsed MW (carrier frequency 3 GHz, pulse repetition 400 Hz, rectangular pulses of 2 μs, power flux density , PD, of 100, 500 and 2500 μW/cm2), during 60 days, 12 h/daily (Koveshnikova and Antipenko 1991) (is a determining factor 1991b). Chromosomal abreactions (CA) were analyzed in hepatocytes. Exposure was performed at three arrays of pulses so that 16, 29 or 48 arrays of pulses per 1 min were generated. The ratio of the obtained doses per animal was 1 : 1.8 : 3, correspondingly. Increased level of CA was generally observed at PD > 100 $\mu W/cm^2$. Importantly, the differences between PD disappeared when the dose per animal increased. In particular, even the PD of 100 μW/cm2 induced CA at higher absorbed doses. These data support the notion that the absorbed dose may be an important parameter for estimation of risks.

Bozhanova with co-authors reported that the effect of cellular synchronization induced by NT MW depended on duration of exposure and PD (Bozhanova, Bryukhova et al. 1987). The dependence on duration of exposure fitted to exponential function. The important observation was that in order to achieve the same synchronization of cells, the decrease in PD could be compensated by the increase in the duration of exposure.

MW exposure of *E. coli* cells and rat thymocytes at PDs of 10^{-5}-10^{-3} W/cm^2 resulted in significant changes in chromatin conformation if exposure was performed at resonance frequencies during 5-10 min (Belyaev, Alipov et al. 1992; Belyaev, Shcheglov et al. 1992; Belyaev and Kravchenko 1994). Decrease in the MW effects due to lowering the PD by orders of magnitude down to 10^{-14}-10^{-17} W/cm^2 could be compensated by several-fold increase of exposure time to 20-40 min (Belyaev, Alipov et al. 1994). At the relatively longer duration of exposure, more then 1 h, and the lowest PD of 10^{-19} W/cm^2, the same effect was induced as at highest PDs and shorter durations (Belyaev, Alipov et al. 1994).

Kwee and Raskmark analyzed effects of MW at 960 MHz and various SARs, 0.021, 0.21, and 2.1 mW/kg on proliferation of human epithelial amnion cells (Kwee and Raskmark 1998). These authors found linear correlations between exposure time to MW at 0.021 and 2.1 mW/kg and the MW-induced changes in cell proliferation albeit no such clear correlation was seen at 0.21 mW/kg.

Peinnequin et al. have studied effects of 24 or 48 h MW 2.45 GHz exposure at non-thermal level, 5 mW/cm^2, on apoptosis in human T-cell line Jurkat clone E6-1 (Peinnequin, Piriou et al. 2000). MW affected Fas -, but neither butyrate- nor ceramide - induced apoptosis. This effect depended on exposure time and was observed only upon 48 h exposure.

Croft et al. have tested twenty-four subjects participated in a single-blind fully counterbalanced cross-over design, where both resting EEG and phase-locked neural responses to auditory stimuli were measured while a mobile phone (MP) was either operating or turned off (Croft, Chandler et al. 2002). MP exposure altered resting EEG, decreasing 1-4 Hz activity (right hemisphere sites), and increasing 8-12 Hz activity as a function of exposure duration. MP exposure also altered early phase-locked neural responses, attenuating the normal response decrement over time in the 4-8 Hz band, decreasing the response in the 1230 Hz band globally and as a function of time, and increasing midline frontal and lateral posterior responses in the 30-45 Hz band. The data have shown that active MPs affect neural function in humans and do so as a function of exposure duration.

Caraglia et al. have evaluated the in vivo effect of MW-EMF in human epidermoid cancer KB cells (Caraglia, Marra et al. 2005). It was found that MW-EMF induced time-dependent apoptosis (45% after 3 h) that was paralleled by an about 2.5-fold decrease of the expression of ras and Raf-1 and of the activity of ras and Erk-1/2.

Gapeyev et al. studied anti-inflammatory effect of low-intensity MW exposure (0.1 mW/cm^2) using the model of acute zymosan-induced footpad edema in mice (Gapeyev, Mikhailik et al. 2008). Single whole-body MW exposure of mice at the frequencies of 42.2, 51.8, and 65 GHz after zymosan injection reduced both the footpad edema and local hyperthermia. At the frequency of 42.2 GHz the effect had sigmoid dependence on exposure duration with a maximum at 20-80 min. A linear dependence on the exposure duration with significantly lower increment was observed at a 10-fold less intensity (0.01 mW/cm^2). However, this decrease in the effect was compensated by a slight increase in duration of exposure from 80 min to 120 min.

Recently, the negative impact of mobile phone usage on semen quality in human males was repeatedly found to correlate with the duration of exposure (Agarwal, Deepinder et al. 2008; Agarwal, Desai et al. 2009).

Gerner et al. exposed human fibroblats to modulated GSM 1800 MHz at 2 W/kg (Gerner, Haudek et al. 2010). While short-term exposure within 2 hours did not significantly alter the proteome, an 8-h exposure caused a significant and reproducible increase in protein synthesis. Most of the proteins found to be induced were chaperones, which are mediators of protein folding. Heat-induced proteome alterations detectable with used proteome methodology would require heating

greater than 1°C. Because GSM-induced heating was less than 0.15°C, a heat-related response was excluded. These data further supported the notion that the exposure time seems to be a critical factor.

Differentiated astroglial cell cultures were exposed for 5, 10, or 20 min to either 900 MHz continuous waves or 900 MHz waves modulated in amplitude at 50 Hz (Campisi, Gulino et al. 2010). The strength of the electric field at the sample position was 10 V/m (rms). The irradiation conditions allowed the exclusion of any possible thermal effect. A significant increase in ROS levels and DNA fragmentation was found only after exposure of the astrocytes to modulated MW for 20 min. No evident effects were detected when shorter time intervals were used.

Adang et al. exposed Wistar albino rats to low-level RF during 21 months to two different microwave frequencies and exposure modes, 2 h a day, seven days a week (Adang, Remacle et al. 2009). After 14 and 18 months of exposure, the authors observed a significant increase in white blood cells and neutrophils of about 15% and 25%, respectively. Lymphocytes fell down after 18 months of exposure with about 15% compared to the sham-exposed group. No effects were observed at shorter duration of exposure. Exposure may probably have worked as a trigger and influenced the immune system, which reacted to this stressor by increasing the percentage of monocytes in the peripheral blood circulation.

Schrader et al. analysed production of spindle disturbances in FC2 cells, a human-hamster hybrid (A(L)) cell line, by MW with a field strength of 90 V/m at a frequency of 835 MHz (Schrader, Munter et al. 2008). Sigmoid dependence on time of exposure was observed with linear increase up to 30 min of exposure and saturation at longer exposures up to 2 h.

Markova et al. have found that inhibitory effect of MW on the 53BP1 foci leveled off at 1h-exposure (Markova, Malmgren et al. 2010). Human mesenchymal stem cells (MSC) and fibroblasts were expsosed to MW at GSM 915 MHz/UMTS 1947 MHz and SAR of 37/39 mW/kg. No further increase in effects was observed both in MSC and fibroblasts at prolongation of exposure to 3 h. This data are in agreement with previous results obtained in human peripheral blood lymphocytes that MW effects were the same at 1-h and 2-h exposures (Belyaev, Hillert et al. 2005; Markova, Hillert et al. 2005).

Panagopoulos and Margaritis have studied the effects of different durations of a single (continuous), daily exposure, ranging from 1 min up to 21 min, to EMF from GSM 900 MHz (Global System for Mobile telecommunications) and DCS 1800 MHz (Digital Cellular System-referred to also as GSM 1800 MHz), on the reproductive capacity of Drosophila melanogaster (Panagopoulos and Margaritis 2010). The insects were exposed to each type of radiation at intensity of about 10 $\mu W/cm^2$, corresponding to a distance of 20 or 30 cm from the antenna of a DCS 1800 or

a GSM 900 mobile phone handset, respectively. The results show that the reproductive capacity decreases almost linearly with increasing exposure duration to both GSM 900 and DCS 1800 radiation, suggesting that short-term exposures to these radiations have cumulative effects. Additionally, the results show that GSM 900 MHz radiation is slightly more bioactive than DCS 1800 MHz radiation, at the same exposure durations and under equal radiation intensities.

In some studies, the prolonged MW exposures were associated with less prominent effects than shorter exposures (Nikolova, Czyz et al. 2005; Tkalec, Malaric et al. 2007; Markova, Malmgren et al. 2010). This type of dependence on exposure duration was explained by adaptation of the exposed biosystems to the MW exposure (Markova, Malmgren et al. 2010).

Esmekaya et al. exposed human peripheral blood lymphocyte to GSM modulated MW radiation at 1.8 GHz and SAR of 0.21 W/kg for 6, 8, 24 and 48 h (Esmekaya, Aytekin et al. 2011). The authors reported morphological changes in exposed lymphocytes. Longer exposure periods led to destruction of organelle and nucleus structures. Chromatin change and the loss of mitochondrial crista occurred in cells exposed to RF for 8 h and 24 h and were more pronounced in cells exposed for 48 h. RF exposure did not increase the temperature. The authors concluded that the greater damage occurred after longer periods of exposure to NT MW.

Tepe Çam and Seyhan have analyzed DNA damage in hair root cells of volunteers before and after they have used 900-MHz GSM mobile phone for 15 or 30 min. The 900-MHz GSM exposure significantly increased single-strand DNA breaks in cells of hair roots close to the position of phone at the heads of volunteers. 30 min talking by mobile phone induced more DNA damage than 15 min talking (Cam and Seyhan 2012).

Nazıroğlu et all have measured cytosolic free Ca^{2+} in human leukemia cells during 1-24 h exposure to 2.45 GHz electromagnetic radiation at the average SAR of 1.63 W/kg (Naziroglu, Cig et al. 2012). Radiation induced increase of cytosolic free Ca^{2+} concentration was time-dependent and was highest at 24-h exposure.

In some studies, prolonged MW exposures were associated with less prominent effects than shorter exposures (Nikolova, Czyz et al. 2005; Tkalec, Malaric et al. 2007; Markova, Malmgren et al. 2010). This type of dependence on exposure duration was accounted for adaptation of the exposed systems to the MW exposure. The magnitude of adaptation depends on a number of biological variables that will be considered elsewhere.

In recent German study, 24 out of 60 participants were exposed to MW from base station at a power density of < 60 μW/m², 20 participants to 60 - 100 μW/m², and 16 participants to more than 100 μW/m² (Buchner and Eger 2011). The values of the stress hormones adrenaline and noradrenaline grew significantly during the first 6 months after starting the GSM base station; the

values of the precursor substance dopamine substantially decreased in this time period. The initial condition was not restored even after 1.5 years. Due to the not regulable chronic difficulties of the stress balance, the phenylethylamine levels dropped until the end of the investigation period. These effects show a dose-effect relationship.

Recently reported general indications of a dose–response relationship between chronic exposure to cellular phone MW and parotid gland malignancy indicate necessity of the dose approach at the epidemiological level (Duan, Zhang et al. 2011). For the first time in epidemiology of RF-induced tumors, Cardis et al. have used estimates of radio frequency energy deposition at the centre of tumors in the brain as a measure of MW dose (Cardis, Armstrong et al. 2011). An increased risk of glioma was seen in individuals at the highest quintile of radio frequency dose, though reduced risks were seen in the four lower quintiles. When risk was examined as a function of dose received in different time windows before diagnosis, an increasing trend was observed with increasing MW dose (for exposures 7 years or more in the past.

In conclusion, the data from different groups suggest that duration of exposure and dose may have significant role for the NT MW effects. In specially designed studies, reduction in dose rate/SAR could be compensated by prolongation of exposure time in order to achieve the same MW effect. The temporal nature of the MW effects contributes to the apparent lack of consistent results reported in the literature. Emerging epidemiology data indicate that the dose of MW exposure may correlate with the increased brain tumor risk.

V. TIME AFTER EXPOSURE

The MW effects on *E. coli* cells significantly depended on the post-exposure time (Belyaev, Shcheglov et al. 1993; Belyaev, Alipov et al. 1994; Shcheglov, Alipov et al. 2002). This dependence had an initial phase of increase about 100 min post-exposure followed by a phase, which was close to a plateau, around 100 min. A trend to decrease in effect was observed at longer times up to 300 min (Belyaev, Shcheglov et al. 1993; Shcheglov, Alipov et al. 2002).

Significant MW-induced changes in chromatin conformation were observed when rat thymocytes were analyzed in-between 30-60 min after exposure to MW (Belyaev and Kravchenko 1994). This effect nearly disappeared if the cells were incubated more than 80 min between exposure and analysis.

Gapeev et al. have studied dependence of the MW effect on the function of the mouse peritoneal neutrophils in dependence on duration of exposure at the frequency of 41.95 GHz and

the PD of 240 μW/cm^2 (Gapeev, Safronova et al. 1996; Gapeyev, Safronova et al. 1997). This dependence had a bell-shaped form with the maximal effects at 20 - 40 min of exposure.

In recent studies, human lymphocytes from peripheral blood of healthy and hypersensitive to EMF persons were exposed to NT MW from the GSM mobile phones (Belyaev, Hillert et al. 2005; Markova, Hillert et al. 2005). NT MW induced changes in chromatin conformation similar to those induced by heat shock, which remained up to 24 h after exposure. It was found in the same and following studies that GSM MW at the carrier frequency of 915 MHz and UMTS (Universal Mobile Telecommunications System) MW at 1947.4 MHz inhibited formation of 53BP1/γ-H2AX DNA repair foci and these adverse effects remained during 72 h after an 1-h exposure (Belyaev, Hillert et al. 2005; Markova, Hillert et al. 2005; Belyaev, Markova et al. 2009). The same group has reported that contrary to human fibroblast, which were able to adapt during chronic exposure to GSM/UMTS non-thermal MW, human stem cells did not adapt (Markova, Malmgren et al. 2010).

Jorge-Mora et al. investigated the effects of MW 2.45 GHz radiation on the paraventricular nucleus (PVN) of the hypothalamus, extracted from brains of exposed rats (Jorge-Mora, Misa-Agustino et al. 2011). Expression of c-Fos was analyzed in rats exposed once or repeatedly (ten times in 2 weeks) to MW at non-thermal SAR of 0.0776 and 0.301 W/kg. High SAR triggered an increase of the c-Fos marker 90 min or 24 h after radiation, and low SAR resulted in c-Fos counts higher than in control rats after 24 h. Repeated irradiation at 0.0776 W/kg increased cellular activation of PVN by more than 100% compared to animals subjected to acute irradiation and to repeated non-radiated repeated session control animals. The results suggest that the time of exposure to single or repeated doses of NT MW is a determining factor, though possibly not the only factor, in establishing the power levels that may produce a response.

Lu et al. have demonstrated that reactive oxygen species (ROS) plays an important role in the process of apoptosis in human peripheral blood mononuclear cell (PBMC), which is induced by the exposure to 900 MHz radiofrequency electromagnetic at the SAR of 0.4W/kg when the exposure lasts longer than two hours (Lu, Huang et al. 2012).

The data indicate that there is a time window for observation of the NT MW effects, which may be dependent on endpoint measured, cell type, duration and PD of exposure.

VI. COHERENCE TIME

MW exposure of L929 fibroblasts was performed by the group of Litovitz (Litovitz, Krause et al. 1993). MW at 915 MHz modulated at 55, 60, or 65 Hz approximately doubled ornithine

decarboxylase (ODC) activity after 8 h. Switching the modulation frequency from 55 to 65 Hz at coherence times of 1.0 s or less abolished enhancement, while times of 10 s or longer provided full enhancement. These results suggested that the microwave coherence effects are remarkably similar to those observed previously with extremely low frequency (ELF) magnetic fields by the same authors.

VII. INTERMITTENCE

Diem and colleagues exposed cultured human diploid fibroblasts and cultured rat granulosa cells to intermittent and continuous MW (1800 MHz; SAR 1.2 or 2 W/kg; different modulations; during 4, 16 and 24 h; intermittent 5 min on/10 min off or continuous exposure) (Diem, Schwarz et al. 2005). Comet assay was applied to analyze DNA single- and double-strand breaks. MW-induced effects occurred after 16 h exposure in both cell types and after different mobile-phone modulations. The intermittent exposure showed a stronger effect than continuous exposure.

Remondini et al. analyzed changes in gene expression in human HL-60 leukemia cells using gene microarrays (Remondini, Nylund et al. 2006). Cells were exposed to MW (SAR 1.0-1.3 W/kg, 1800 MHz DTX mode, 24 h exposure) either continuously or intermittently, 5 min ON/5 min OFF. Gene expression was affected by intermittent exposure but not continuous exposure.

Elhag et al. investigated effect of near field EMR from GSM mobile phones on the oxidant and antioxidant status in rats (Elhag, Nabil et al. 2007). Rats were subjected to either intermittent exposure (15 min/day for four days) or acute exposure for 1 h. Significant drop in the plasma concentration of vitamin C, vitamin E, vitamin A and reduced glutathione (GSH) was observed in both exposed groups as compared to controls. EMR exposure of rats produced a significant decrease in catalase (CAT) and superoxide dismutase (SOD) activities, with the values of these activities for acute-exposure group is significantly lower than those of intermittent exposure. The authors concluded that the effects of acute exposure to mobile phones on the rat's antioxidant status is significantly higher than those of intermittent exposure of the same type of radiation.

Chavdoula et al used a 6-min daily exposure of dipteran flies, Drosophila melanogaster, to GSM-900MHz (Global System for Mobile Telecommunications) mobile phone electromagnetic radiation (EMR), to compare the effects between the continuous and four different intermittent exposures of 6 min total duration on the insect's reproductive capacity as well as on the induction of apoptosis (Chavdoula, Panagopoulos et al. 2010). It was found that intermittent exposure, similar to continuous exposure, decreases the reproductive capacity and alters the actin-cytoskeleton network

of the egg chambers, another known aspect of cell death, and that this effect is due to DNA fragmentation. Intermittent exposures with 10-min intervals between exposure sessions proved to be almost equally effective as continuous exposure of the same total duration, whereas longer intervals between the exposures seemed to allow the organism the time required to recover and partly overcome the above-mentioned effects of the GSM exposure.

VIII. MODULATION

Several types of modulations used in mobile communication have previously been reviewed (Foster and Repacholi 2004; Blackman 2009; Juutilainen, Hoyto et al. 2011). In particular, the 2G signals use the Gaussian Minimum Shift Keying (GMSK) modulation, have a high coherence, extremely low frequency amplitude modulation spectra, high crest factor (pulsed signal) and a power regulation with an update in the order of seconds. In contrast, the 3G Wideband Code-Division Multiple Access (WCDMA) uses essentially Quadrature Phase Shift Keying (QPSK) modulation, has a low coherence and a broad-band extremely low frequency amplitude modulation spectrum.

While considering effect of modulation, all other parameters, which are important for appearance of biological effects induced by NT MW, should be taken into account. In particular it is useless to include in analysis the papers where no effects of NT MW were detected at all because usually these studies do not scan the parameters of exposure in wide range to enable detecting the NT MW effects. Even more importantly is to analyze separately different types of modulations because each type may result in its own specific effect. When such approach is used, clear evidence is emerging for the effects of specific modulations. For example, among three studies on cancer-relevant non-genotoxic endpoints, biological effects (apoptosis, altered cell proliferation, lipid peroxidation) were induced by GSM modulated signal but not by a CW signal (Juutilainen, Hoyto et al. 2011). All these studies involved combined exposure to RF fields and other agents, and found GSM-modulation-specific effects on apoptosis. Another example is increased power in the alpha band (8–12 Hz) of EEG, which has been consistently seen in several studies most of which have used GSM-type modulation and have found that signals with pulse modulation are more biologically active than CW fields, or that signals with higher degree of modulation (e.g., handset-like signals) are more biologically active than signals with lower degree of modulation (e.g., base station-like signals). Studies that have used only GSM-type signals have provided additional evidence for effects of modulated RF signals on human brain functions (van Rongen, Croft et al.

2009). Overall, the consistency of the positive findings indicates that there may be reproducible modulation-specific effects on the human central nervous system (Juutilainen, Hoyto et al. 2011). This result is consistent with the well-known notion that properly modulated RF may be a useful tool in experiments directed at understanding nervous system function (Frey 1967).

Using aforementioned approach, it became clear that significant body of papers where NT MW effects were observed and modulated and unmodlatlated signals were carefully compared revealed the differences. There is strong experimental evidence for the role of modulation in the diverse biological effects of NT MW both in vitro and in vivo (Lin-Liu and Adey 1982; Byus, Lundak et al. 1984; Dutta, Subramoniam et al. 1984; Byus, Kartun et al. 1988; Dutta, Ghosh et al. 1989; Veyret, Bouthet et al. 1991; Gapeev, Iakushina et al. 1997; Litovitz, Penafiel et al. 1997; Penafiel, Litovitz et al. 1997; Persson, Salford et al. 1997; d'Ambrosio, Massa et al. 2002; Huber, Treyer et al. 2002; Markkanen, Penttinen et al. 2004; Huber, Treyer et al. 2005). Examples include different types of modulation such as amplitude-, speech and phase modulations: (i) Amplitude modulation at 16 Hz, but not 60 Hz or 100 Hz, of a 450-MHz MW increased activity of ODC (Byus, Kartun et al. 1988). (ii) Speech-modulated 835-MHz MW produced no effect on ODC as compared to the typical signal from a TDMA (Time Division Multiple Access) digital cellular phone (Penafiel, Litovitz et al. 1997). (iii) Phase-modulated GSM-1800 MW (Gaussian Minimum Shift Keying, GMSK) at 1.748 GHz induced micronuclei in human lymphocytes while CW MW did not (d'Ambrosio, Massa et al. 2002).

Normal human lymphocytes were exposed for 5 days to continuous wave (CW) or pulsed wave (PW) 2450-MHz radiation at non-heating (37 degrees C) and various heating levels (temperature increases of 0.5, 1.0, 1.5, and 2 degrees C) (Czerska, Elson et al. 1992). The pulsed exposures involved 1-microsecond pulses at pulse repetition frequencies from 100 to 1,000 pulses per second at the same average SAR levels as the CW exposures. At non-heating levels, CW exposure did not affect lymphoblastoid transformation. At heating levels both conventional and CW heating enhanced transformation to the same extent and correlate with the increases in incubation temperature. PW exposure enhanced significantly transformation at non-heating levels. At heating levels PW exposure enhanced transformation to a greater extent than did conventional or CW heating. Authors concluded that PW 2450-MHz radiation acts differently on the process of lymphoblastoid transformation in vitro compared with CW 2450-MHz radiation at the same average SARs.

Bolshakov and Alexeeev used microelectrode and voltage-clamp techniques to record spontaneous electrical activity and ionic currents of Lymnea stagnalis neurons during exposure to a 900-MHz field in a waveguide-based apparatus (Bolshakov and Alekseev 1992). The field was

pulse-modulated at repetition rates ranging from 0.5 to 110 pps, or it was applied as a continuous wave (CW). When subjected to pulsed waves (PW), rapid, burst-like changes in the firing rate of neurons occurred at SARs of a few W/kg. If the burst-like irregularity was present in the firing rate under control conditions, irradiation enhanced its probability of occurrence. The effect had a threshold SAR near 0.5 W/kg. CW radiation had no effect on the firing rate pattern at the same SAR. Thus, the effect was dependent on modulation. Mediator-induced, current activation of acetylcholine, dopamine, serotonin, or gamma-aminobutyric-acid receptors of the neuronal soma was not altered during CW or PW exposures and, hence, could not have been responsible for the bursting effect.

Gapeev and co-authors studied production of reactive oxygen species (ROS) in isolated peritoneal neutrophils of mice using a model of synergistic reaction of calcium ionophore A23187 and phorbol ester PMA (Gapeev, Iakushina et al. 1997; Gapeyev, Yakushina et al. 1998). MW exposure at 41.95 GHz, continuous wave mode and 50 $\mu W/cm^2$, inhibited ROS production. MW modulated with the frequency of 1 Hz resulted in stimulation of the synergistic reaction. Modulation frequencies of 0.5, 2, 4, and 8 Hz did not cause significant effects, and modulation frequencies of 0.1, 16, and 50 Hz inhibited the synergistic reaction.

In other study, Gapeev et al. analyzed acute zymosan-induced paw edema in mice (Gapeyev, Mikhailik et al. 2009). MW exposure of animals at the PD of 0.1- 0.7 mW/cm^2 and some "effective" frequencies in the range of 42-43 GHz decreased the paw edema. Application of different modulation frequencies from the range of 0.03–100 Hz to MW exposure at the effective carrier frequency of 42.2 GHz did not lead to considerable changes in the effect. In contrast, modulation of MW at the ''ineffective'' carrier frequencies of 43.0 and 61.22 GHz by frequencies from the ranges of 0.07–0.1 and 20–30 Hz resulted in a maximal anti-inflammatory effects. The results suggested a complex dependence of the anti-inflammatory action of low-intensity MW on carrier and modulation frequencies.

Capri et al. evaluated the nonthermal effects of both a 900 MHz GSM signal and a 900 MHz CW RF field at low SARs (70–76 mW/kg average) on human peripheral blood mononuclear cells (PBMCs) *in vitro* (Capri, Scarcella et al. 2004). Data obtained from cells exposed to a GSM-modulated RF field showed a slight decrease in cell proliferation when PBMCs were stimulated with the lowest mitogen concentration and a slight increase in the number of cells with altered distribution of phosphatidylserine across the membrane. Data obtained from CW-exposed cultures showed no difference with respect to sham-exposed cultures in any of the end points studied.

Huber with coauthors investigated effects of MW similar to those used in mobile communication, a "base-station-like" and a "handset-like" signal (10 g tissue-averaged spatial peak-

SAR of 1 W/kg for both conditions), on waking regional cerebral blood flow (rCBF) in 12 healthy young men (Huber, Treyer et al. 2005). The effect depended on the spectral power in the amplitude modulation of the carrier frequency such that only "handset-like" MW exposure with its stronger low-frequency components but not the "base-station-like" MW exposure affected rCBF. This finding supported previous observations of these authors (Huber, Treyer et al. 2002) that pulse modulation of MW is of importance for changes in the waking and sleep EEG, and substantiated the notion that pulse modulation is crucial for MW-induced alterations in brain physiology.

Markkanen et al. exposed cdc48-mutated *Saccharomyces cerevisiae* yeast cells to 900 or 872 MHz MW, with or without exposure to ultraviolet (UV) radiation, and analyzed apoptosis (Markkanen, Penttinen et al. 2004). Amplitude modulated (217 pulses per second) MW significantly enhanced UV induced apoptosis in cells, but no effect was observed in cells exposed to unmodulated fields at the identical time-average SAR of 0.4 W/kg that was lower than the ICNIRP safety standards.

Persson and colleagues studied effects of MW of 915 MHz as CW and pulse-modulated with different pulse power and at various time intervals on permeability of the blood-brain barrier (BBB) in Fischer 344 rats (Persson, Salford et al. 1997). Albumin and fibrinogen were demonstrated immunochemically and classified as normal versus pathological leakage. The CW-pulse power varied from 0.001 W to 10 W and the exposure time from 2 min to 960 min. The frequency of pathological rats significantly increased in all exposed rats. Grouping the exposed animals according to the level or specific absorption energy (J/kg) gave significant difference in all levels above 1.5 J/kg. The exposure was 915 MHz MW either pulse modulated at 217 Hz with 0.57 ms pulse width, at 50 Hz with 6.6 ms pulse width, or CW. The frequency of pathological rats was significantly higher in MW-exposed groups than in controls and the frequency of pathological rats after exposure to pulsed radiation was significantly less than after exposure to CW.

In a study by Lypez-Martin et al. (Lopez-Martin, Brogains et al. 2009), GSM-exposed picrotoxin-pretreated rats showed differences in clinical and EEG signs, and in c-Fos expression in the brain, in comparison to picrotoxin-treated rats exposed to an equivalent dose of unmodulated radiation. Neither MW exposure caused tissue heating, so thermal effects could be ruled out. The most marked effects of GSM MW on c-Fos expression in picrotoxin-treated rats were observed in limbic structures, olfactory cortex areas and subcortical areas, the dentate gyrus, and the central lateral nucleus of the thalamic intralaminar nucleus group. Nonpicrotoxin-treated animals exposed to unmodulated radiation showed the highest levels of neuronal c-Fos expression in cortical areas. These results suggested a specific effect of the pulse GSM modulation on brain activity of a picrotoxin-induced seizure-proneness rat model.

Luukkonen et al. investigated effects of MW at 872 MHz and relatively high SAR value (5 W/kg) on intracellular reactive oxygen species (ROS) production and DNA damage in human SH-SY5Y neuroblastoma cells. The experiments also involved combined exposure to MW and menadione, a chemical inducing intracellular ROS production and DNA damage. Both CW and a pulsed signal similar to that used in GSM mobile phones were used. Exposure to the CW radiation increased DNA breakage in comparison to the cells exposed only to menadione. Comparison of the same groups also showed that ROS level was higher in cells exposed to CW RF radiation at 30 and 60 min after the end of exposure. No effects of the GSM-like modulated signal were seen on either ROS production or DNA damage.

Hinrikus et al. (Hinrikus, Bachmann et al. 2008) evaluated the effects of MW (450 MHz) pulse-modulated at the frequencies of 7, 14 and 21 Hz on human electroencephalographic (EEG) rhythms. The field power density at the scalp was 0.16 m W/cm^2. Modulated microwaves caused an increase in the average EEG alpha (17%) and beta (7%) power but the theta rhythm remained unaffected. Increases in the EEG alpha and beta power were statistically significant during the first half-period of the exposure interval (30 s) at the modulation frequencies of 14 and 21 Hz. The authors concluded that the effect of the 450-MHz MW modulated at 7, 14 and 21 Hz varies depending on the modulation frequency.

Hoyto et al. exposed human SH-SY5Y neuroblastoma and mouse L929 fibroblast cells to MW (SAR of 5 W/kg) at 872 MHz using continuous-waves (CW) or a modulated GSM-like signal under isothermal conditions (Hoyto, Luukkonen et al. 2008). Menadione was used to induce reactive oxygen species, and tert-butylhydroperoxide (t-BOOH) was used to induce lipid peroxidation. Two statistically significant differences related to MW exposure were observed: Lipid peroxidation induced by t-BOOH was increased in SH-SY5Y (but not in L929) cells, and menadione-induced caspase 3 activity was increased in L929 (but not in SH-SY5Y) cells. Both differences were statistically significant only for the GSM-modulated signal.

Franzellitti et al. exposed human trophoblast HTR-8/SVneo cells to MW at 1.8 GHz CW and differently modulated GSM signals (GSM-217Hz, (speaking only): and GSM-Talk (34% of speaking and 66% of hearing):) during 4 - 24 h (Franzellitti, Valbonesi et al. 2008). The inducible HSP70C transcript was significantly enhanced after 24 h exposure to GSM-217 Hz signals while being reduced after 4 and 16 h exposure to GSM-Talk signal. In another study of the same group , HTR-8/SVneo cells were exposed for 4, 16 or 24 h to 1.8 GHz continuous wave (CW) and different GSM signals, namely GSM-217 Hz and GSM-Talk (intermittent exposure: 5 min field on, 10 min field off). The alkaline comet assay was used to evaluate primary DNA damages and/or strand breaks due to uncompleted repair processes in HF-EMF exposed samples. The amplitude-

modulated signals GSM-217 Hz and GSM-Talk induced a significant increase in comet parameters in trophoblast cells after 16 and 24 h of exposure, while the un-modulated CW was ineffective (Franzellitti, Valbonesi et al. 2010).

Only CW RF resulted in statistically significant effect on immune system of the exposed rats (Campisi, Gulino et al. 2010). In this study, primary rat neocortical astroglial cell cultures were exposed to MW for 5, 10, or 20 min to either 900 MHz continuous waves or 900 MHz waves modulated MW in amplitude at 50 Hz using a sinusoidal waveform and 100% modulation index. The strength of the electric field (rms value) at the sample position was 10 V/m. A significant increase in ROS levels and DNA fragmentation was found only after exposure of the astrocytes to modulated EMF for 20 min. No evident effects were detected when shorter time intervals or continuous waves were used. The irradiation conditions allowed the exclusion of any possible thermal effect. The results show the importance of the amplitude modulation in the interaction between EMF and neocortical astrocytes (Campisi, Gulino et al. 2010).

There are studies where similar effects of modulated and CW MW were observed. Adang et al. exposed Wistar albino rats to low-level CW and pulse-amplitude modulated RF during 21 months at 970 MHz (Adang, Remacle et al. 2009). Similar effects on immune system were observed in both groups.

Significant amount of *in vivo* studies under varying parameters of exposure (intensity, frequency, exposure time, modulation, intermittence) have been performed in Russia/Soviet Union and published in Russian. Retrospective analysis of 52 Russian/Soviet *in vivo* studies with animals (mice, rats, rabbits, guinea pigs) on chronic exposure to MW has recently been published (Grigoriev, Stepanov et al. 2003). In these studies, various endpoints were measured up to 4 month of chronic exposure including analysis of: weight of animal body, histological analysis and weight of tissues, central nervous system, arterial pressure, blood and hormonal status, immune system, metabolism and enzymatic activity, reproductive system, teratogenic and genetic effects. Based on their analysis, the authors concluded that: “exposure to modulated MW resulted in bioeffects, which can be different from the bioeffects induced by CW MW; exposure to modulated MW at low intensities (non-thermal levels) could result in development of unfavorable effects; direction and amplitude of the biological response to non-thermal MW, both *in vitro* and *in vivo*, depended on type of modulation; often, but not always, modulated MW resulted in more pronounced bioeffects than CW MW; the role of modulation was more pronounced at lower intensity levels”.

One review of the Russian/Soviet studies on the role of modulation on MW effects is available in English (Pakhomov and Murphy 2000). The authors conclude that “a number of good-quality studies have convincingly demonstrated significant bioeffects of pulsed MW. Modulation

often was the factor that determined the biological response to irradiation, and reactions to pulsed and CW emissions at equal time-averaged intensities in many cases were substantially different". Since that time, more studies have been published in Russian which show the role of modulation in experiemnts with animals (Dolgacheva, Semenova et al. 2000; Pashovkina and Akoev 2000; Pashovkina and Akoev 2001; Pashovkina and Akoev 2001; Akoev, Pashovkina et al. 2002).

In conclusion, significant amount of in vitro and in vivo studies from different research groups, although not universally reported, clearly indicated dependence of the NT MW effects on modulation.

IX. POLARIZATION

Polarization is a property of electromagnetic waves that describes the orientation of their oscillations versus direction of propagation. In most cases, electromagnetic wave propagates in free space as a transverse wave - the polarization is perpendicular to the wave's direction of propagation. The electric field may be oriented in a single direction (linear polarization), or it may rotate as the wave propagates (circular or elliptical polarization). In the latter cases, the oscillations can rotate either towards the right (right-handed polarization) or towards the left (left-handed polarization) in the direction of propagation.

The effects of circularly polarized (CP) MW were studied in *E. coli* cells at the frequencies from two frequency windows (resonances) that were identified using linearly polarized (LP) MW, within the frequency ranges of 51.62-51.84 GHz and 41.25-41.50 GHz (Belyaev, Alipov et al. 1992; Belyaev, Shcheglov et al. 1992). At the resonance frequency of 51.76 GHz, right-handed CP MW inhibited repair of X-ray-induced DNA damages (Belyaev, Alipov et al. 1992; Belyaev, Shcheglov et al. 1992). In contrast to right-handed polarization, left-handed CP MW had virtually no effect on the DNA repair, while the efficiency of LP MW was in-between of two circular polarizations. Inversion in effectiveness of circular polarizations was observed at another resonance frequency, 41.32 GHz. In contrast to the frequency of 51.76 GHz, left-handed CP MW at 41.32 GHz significantly inhibited DNA repair, while right polarization was almost ineffective. MW of the same CP affected cells at several frequencies tested within each resonance, alternative CP being almost ineffective (Belyaev, Alipov et al. 1992; Belyaev, Shcheglov et al. 1992; Belyaev, Shcheglov et al. 1992). Therefore, specific sign of effective CP, either left- or right-, was the attribute of each resonance. Two different types of installations, based on either spiral waveguides (Belyaev, Shcheglov et al. 1992) or quarter-wave mica plates (Belyaev, Alipov et al. 1992; Belyaev,

Shcheglov et al. 1992; Shcheglov, Belyaev et al. 1997; Ushakov, Shcheglov et al. 1999; Ushakov, Alipov et al. 2005), were used to produce CP MW. Similar results were observed regardless the way of producing the MW of different polarizations.

Pre-irradiation of *E. coli* cells to X-rays inverted the sign of effective polarization (Belyaev, Alipov et al. 1992; Belyaev, Shcheglov et al. 1992). This inversion was observed for two different resonances, 41.32 and 51.76 GHz. Neither resonance frequencies, nor half-widths of the resonance changed during the inversions in effective CPs. The effects of left- and right-handed CP MW become the same at 50 cGy (Belyaev, Alipov et al. 1992). At this dose, about one single stranded DNA break per haploid genome was induced. X-ray-induced DNA breaks result in relaxation of the supercoiled DNA-domains. It is known that the majority of DNA in living cells has a right-handed helicity (B-form) but a minor part, in order of 1 %, may alternate from the B-form with the form of left-handed helix (Z-form). Supercoiling is connected with transitions between right B-form to left Z-form in these DNA sequences. Therefore, the data suggested that difference in biological effects of polarized MW might be connected with DNA helicity and supercoiling of DNA-domains.

Supercoiling of DNA-domains is changed during cell cycle because of transcription, replication, repair, and recombination. It can also be changed by means of DNA-specific intercalators such as ethidium bromide (EtBr). EtBr changes supercoiling and facilitates the transition of DNA sequences from Z-form to B-form. Preincubation of *E. coli* AB1157 cells with EtBr inverted the effective polarization at the resonance frequency of 51.755 GHz and right-handed MW became more effective than left polarization (Ushakov, Shcheglov et al. 1999). EtBr changed the supercoiling of DNA-domains starting at a concentration of 1 μg/ml as measured with the AVTD in different cell types including *E. coli* (Belyaev, Shcheglov et al. 1996; Belyaev, Alipov et al. 1997; Belyaev, Eriksson et al. 1999). These data provided further evidence that DNA may be a target for the NT MW effects.

The effects of MW on conformation of nucleoids in *E. coli* cells have recently been studied at the power flux density of 100 $\mu W/cm^2$ (Ushakov, Alipov et al. 2006). Linearly polarized MW resulted in significant effects within specific frequency windows of resonance type in the range of 51-52 GHz. The distances between frequency windows were about 55-180 MHz. Only one of the two possible circular polarizations, left-handed or right-handed, was effective at each frequency window. The sign of effective circular polarization alternated between frequency windows.

While most data on the role of polarization in MW effects on chromatin have been obtained by the same research group (Belyaev, Alipov et al. 1992; Belyaev, Shcheglov et al. 1992; Belyaev, Shcheglov et al. 1992; Alipov, Belyaev et al. 1993; Belyaev, Alipov et al. 1993; Belyaev, Shcheglov et al. 1993; Belyaev and Kravchenko 1994; Shcheglov, Belyaev et al. 1997; Ushakov,

Shcheglov et al. 1999; Ushakov, Alipov et al. 2005; Ushakov, Alipov et al. 2006), recent data of others corroborated our findings at least partially (Shckorbatov, Pasiuga et al. 2009). These authors analyzed the condensation of chromatin in human buccal epithelium cells and human fibroblasts by the method of vital indigo carmine staining. MW induced chromatin condensation in dependence on polarization (Shckorbatov, Pasiuga et al. 2009). The same research group investigated the effects influence of linear and left-handed and right-handed elliptically polarized MW at 36.65 GHz on chromatin in human fibroblast nuclei (Shckorbatov, Pasiuga et al. 2010). Microwave irradiation at 10 and 100 $\mu W/cm^2$ induced chromatin condensation. The right-handed elliptically polarized radiation was more active than the left-handed polarization.

Obviously, the difference in effects of right- and left polarizations could not be explained by the heating or by the mechanism dealing with "hot-spots" due to unequal SAR distribution. The data about the difference in effects of differently polarized MW, the inversion of effective circular polarization between resonances and after irradiation of cells with X-rays and incubation with EtBr provided strong evidence for the non-thermal mechanisms of MW effects. These data suggested chiral asymmetry in the target for the NT MW effects, one of which is presumably chromosomal DNA (Belyaev, Alipov et al. 1992), and selection rules on helicity if quantum-mechanical approach is applied (Belyaev, Shcheglov et al. 1992).

Lai and Singh have consistently reported that circularly polarized MW exposure at 2450 MHz induced DNA damage in brain cells of the exposed rats (Lai and Singh 1995; Lai and Singh 1996; Lai and Singh 1997). Replication studies have also tested circularly polarized MW exposure at 2450 MHz and no induced DNA damage was reported (Malyapa, Ahern et al. 1997; Malyapa, Ahern et al. 1998; Lagroye, Anane et al. 2004). All these replication studies have used another exposure system. However, handedness of circular polarization has not been described neither in original study, no in replications. If the handedness was different between studies it could reasonably account for inconsistency.

In some studies, MW of circular polarization with undefined handedness were used, but the obtained effects were not compared with alternative circular polarization or linear polarization (Bartsch, Kupper et al. 2010).

XI. ELECTROMAGNETIC ENVIRONMENT

It is very likely that background EMF might be of importance for the MW effects. This hypothesis is based on the experimental observations that SMF, ELF magnetic fields, and MW at

low intensities induced similar effects in cells under specific conditions of exposure (Belyaev, Alipov et al. 1999; Belyaev, Shcheglov et al. 2000; Belyaev and Alipov 2001; Binhi, Alipov et al. 2001; Belyaev, Hillert et al. 2005). Despite very little has been achieved for mechanistic explanation of such effects, there are attempts to consider the effects of EMF in a wide frequency range in the frames of the same physical models (Chiabrera, Bianco et al. 1991; Matronchik, Alipov et al. 1996; Chiabrera, Bianco et al. 2000; Binhi 2002; Panagopoulos, Karabarbounis et al. 2002; Matronchik and Belyaev 2005; Matronchik and Belyaev 2008).

Litovitz and colleagues found that the ELF magnetic noise inhibited the effects of MW on ODC in L929 cells (Litovitz, Penafiel et al. 1997). The ODC enhancement was found to decrease exponentially as a function of the noise root mean square amplitude. With 60 Hz amplitude-modulated MW, complete inhibition was obtained with noise levels at or above 2 μT. With the DAMPS (Digital Advanced Mobile Phone System) cellular phone MW, complete inhibition occurred with noise levels at or above 5 μT. Further studies by the same group revealed that the superposition of ELF noise inhibited hypoxia de-protection caused by long term repeated exposures of chick embryos to MW (Di Carlo, White et al. 2002).

The effect of a magnetic noise on microwave-induced spatial learning deficit in the rat was investigated by Lai (Lai 2004). Rats were exposed to MW (2450 MHz CW, PD 2 mW/cm^2, average whole-body SAR 1.2 W/kg) alone or in combination with noise exposure (60 mG). Microwave-exposed rats had significant deficit in learning. Exposure to noise alone did not significantly affect the performance of the animals. However, simultaneous exposure to noise significantly attenuated the microwave-induced spatial learning deficit. The author concluded that simultaneous exposure to a temporally incoherent magnetic field blocks MW-induced spatial learning and memory deficits in the rat (Lai 2004).

Lai and Singh studied combined effects of a temporally incoherent magnetic noise (45 mG) and MW (CW 2450 MHz, PD 1 mW/cm^2, average whole-body SAR of 0.6 W/kg) in rat brain cells (Lai and Singh 2005). MW exposure induced significant DNA breakages as measured with both neutral and alkaline comet assays. Exposure to noise alone did not significantly affect cells. However, simultaneous noise exposure blocked the MW-induced effects.

Burch et al. have analyzed the relationship between cellular telephone use and excretion of the melatonin metabolite 6-hydroxymelatonin sulfate (6-OHMS) in two populations of male electric utility workers (Study 1, *n*=149; Study 2, *n*=77) (Burch, Reif et al. 2002). Participants collected urine samples and recorded cellular telephone use over 3 consecutive workdays. Personal 60-Hz magnetic field (MF) and ambient light exposures were characterized on the same days. A repeated measures analysis was used to assess the effects of cellular telephone use, alone and combined with

MF exposures, after adjustment for age, participation month and light exposure. No change in 6-OHMS excretion was observed among those with daily cellular telephone use >25 min in Study 1 (5 worker-days). Study 2 workers with >25 min cellular telephone use per day (13 worker-days) had lower creatinine-adjusted mean nocturnal 6-OHMS concentrations (p=0.05) and overnight 6-OHMS excretion (p=0.03) compared with those without cellular telephone use. There was also a linear trend of decreasing mean nocturnal 6-OHMS/creatinine concentrations (p=0.02) and overnight 6-OHMS excretion (p=0.08) across categories of increasing cellular telephone use. A combined effect of cellular telephone use and occupational 60-Hz MF exposure in reducing 6-OHMS excretion was also observed in Study 2. The authors concluded that exposure-related reductions in 6-OHMS excretion were observed in Study 2, where daily cellular telephone use of >25min was more prevalent. Prolonged use of cellular telephones may lead to reduced melatonin production, and elevated 60-Hz MF exposures may potentiate the effect.

Yao and colleagues investigated the influence of the GSM-like MW at 1.8 GHz on DNA damage and intracellular reactive oxygen species (ROS) formation in human lens epithelial cells (hLECs) (Yao, Wu et al. 2008). DNA damage examined by alkaline comet assay was significantly increased after 3 W/kg and 4 W/kg radiation, whereas the double-strand breaks (DSB) evaluated by γ-H2AX foci were significantly increased only after 4 W/kg radiation. Significantly elevated intracellular ROS levels were detected in the 3-W/kg and 4-W/kg groups. After exposure to 4 W/kg for 24 hours, hLECs exhibited significant G_0/G_1 arrest. All the effects were blocked when the MW exposure was superposed with a 2 μT electromagnetic noise. The authors concluded that superposed electromagnetic noise blocks MW-induced DNA damage, ROS formation, and cell cycle arrest.

It has previously been reported that resonance effects of MW on *E. coli* cell depend on the magnitude of static magnetic field at the place of MW exposure (Belyaev, Alipov et al. 1994). This dependence was explained by the model of electron-conformational interactions that also predicted possible shift of resonance frequencies in dependence on SMF (Belyaev, Shcheglov et al. 1996).

More recently, Ushakov with co-authors exposed *E. coli* cells to MW at the PD of 10^{-10} W/cm^2 and the frequencies of 51.675, 51.755 and 51.835 GHz (Ushakov, Alipov et al. 2005). In this study, cells were exposed to MW at various values of SMF within the range of geomagnetic filed: 22, 49, 61, or 90 μT. The authors observed that the effects of MW exposure on the conformation of nucleoids depended on the SMF during exposure.

Gapeev at al. analyzed effects of MW (41.85-42.1 GHz, frequency increment 50 MHz, PD 50 μВт/cm^2, 20 min exposure) on synergistic reaction of calcium ionophore A23187 and phorbol ester PMA in activation of the respiratory burst of the peritoneal neutrophils of mice (Gapeev,

Iakushina et al. 1997). The MW exposure was performed at various SMF. At a SMF of 50 μT, the authors observed frequency-dependent inhibition of the synergetic reaction with maximal effect at the frequency of 41.95 GHz. In the same frequency range, frequency-dependent activation of the synergetic reaction with a maximal effect at the frequency of 42.0 GHz was found at a SMF of 95 μT. The authors concluded that increasing the SMF from 50 to 95 μT resulted in the inversion of ten MW effects and the shift of the resonance frequency by 50 MHz (Gapeev, Iakushina et al. 1997; Gapeev, Iakushina et al. 1999). Moreover, these effects of MW at the 41.95 GHz and 42.0 GHz were not found at the SMF of ±1, 28.3, 75.5 or 117.3 μT suggesting that the NT MMW effects may appear only at specific values of SMF (Gapeev, Iakushina et al. 1997; Gapeev, Iakushina et al. 1999).

During 1997–2008, Bartsch et al. have performed two long-term (I and II) and two life-long (III and IV) experiments analyzing the effect of chronic exposure to a low-intensity GSM-like signal (900 MHz pulsed with 217 Hz, 100 μW/cm² average power flux density, 38–80 mW/kg SAR for whole body) on health and survival of unrestrained female Sprague-Dawley rats kept under identical conditions (Bartsch, Kupper et al. 2010). Radiofrequency continued up to 37 months. In experiment I no adverse health effects of chronic RF-exposure were detectable, neither by macroscopic nor detailed microscopic pathological examinations. Also in experiment II no apparent macroscopic pathological changes due to treatment were apparent. In the course of two complete survival experiments (2002–2005; 2005–2008) median survival was significantly shortened under RF-exposure in both experiments by 9.06% (95% CI 2.7 to 15.0%) (p=0.0064); i.e by 72 days in experiment III and 77 days in experiment IV (Bartsch, Kupper et al. 2010). Based on their thorough analysis of possible reasons for variability in RF effects from year to year, the authors assumed that theses variations follow the course of solar activity within the 11-years' sunspot cycle which, according to theirs reported observations, seems to affect pineal melatonin secretion which is an integral part of endogenous defense against cancer. The activity of the sun may influence laboratory animals via changes in the geomagnetic field, which is omnipresent and perceived by specific receptors, e.g. retinal melanopsin, also involved in the light-mediated synchronization of the SCN (central circadian clock of the brain) and controlling the circadian secretion of pineal melatonin.

The observations indicating dependence of the NT MW effects on SMF and EMF stray field may be of significant interest for further development of physical theory for the NT MW effects and development of safe mobile communication.

XII. CELL-TO-CELL INTERACTION IN RESPONSE TO MICROWAVES

The effects of NT MW at the resonance frequency of 51.755 GHz on conformation of nucleoids in *E. coli* cells were analyzed with respect to cell density during exposure (Belyaev, Alipov et al. 1994). The per-cell-normalized effect of MW increased by a factor of 4.7±0.5 on average if cell density increased by one order of magnitude, from $4 \cdot 10^7$ to $4 \cdot 10^8$ cell/ml. These data suggested a co-operative nature of cell response to MW, which is based on cell-to-cell interaction during exposure. This suggestion was in line with the observed partial synchronization of cells after exposure to MW.

The co-operative nature of cell response to MW at the resonance frequency of 51.755 GHz was confirmed in further studies with *E. coli* cells (Belyaev, Shcheglov et al. 1996; Shcheglov, Belyaev et al. 1997; Shcheglov, Alipov et al. 2002). In addition, dependence of the per-cell-normalized effect on cell density was found for two other resonances, 51.675 GHz and 51.688 GHz. These data suggested that dependence on cell density during exposure is a general attribute of the resonance response of *E. coli* cells to NT MW. At the cell density of $4 \cdot 10^8$ cells/ml, the average intercellular distance was approximately 13 μm that is 10 times larger than the linear dimensions of *E. coli* cells (Belyaev, Alipov et al. 1994; Shcheglov, Alipov et al. 2002). Therefore, no direct physical contact seemed to be involved in the cell-to-cell interaction. Two mechanisms, biochemical and electromagnetic, were considered to account for the co-operative nature in the resonance response to weak EMF in wide frequency range including ELF, MW and ionizing radiation (Belyaev 1993; Belyaev, Alipov et al. 1994; Alipov, Shcheglov et al. 2003). The first one, biochemical, is based on release of secondary chemical messengers (ions, radicals, or molecules) by those cells, which were directly targeted. Via diffusion, these messengers can induce response in other cells. The second mechanism, electromagnetic, is based on reemission of secondary photons. According to this mechanism, reemitted photons can induce response in other cells if the intercellular distance is shorter than the length of photon absorption. The experimental data on MW effects fitted better to the electromagnetic mechanism but a combination of two mechanisms was also possible (Belyaev, Alipov et al. 1994; Shcheglov, Alipov et al. 2002). In particular, radicals with prolonged lifetimes might be involved in the observed cell-to-cell communication during response to EMF (Belyaev, Alipov et al. 1998).

The absorption length of photons with the frequencies of 10^{12}-10^{13} Hz corresponds to the intracellular distance at the cell density of $5 \cdot 10^8$ cell/ml, at which saturation in the dependences of EMF effects on cell density was observed (Belyaev, Alipov et al. 1994; Belyaev, Alipov et al. 1995; Belyaev, Alipov et al. 1998; Shcheglov, Alipov et al. 2002). Such photons may be involved in cell-

to-cell communication according to the electromagnetic mechanism and in agreement with the prediction of Fröhlich that biosystems support coherent excitations within frequency range of 10^{11}-10^{12} Hz (Frohlich 1968). From this point of view, cell suspension may respond to NT MW as a whole. In this case, the number of the exposed cells should be large enough to facilitate cell-to-cell communication during the responses to MW at specific parameters of exposure such as frequency, modulation, and polarization. Interestingly, the cell density for saturation of both MW and ELF effects was about $5 \cdot 10^8$ cell/ml that is close to cell densities in soft tissues of eukaryotes (Belyaev, Alipov et al. 1998; Shcheglov, Alipov et al. 2002). Such density of cells in the tissues may be important for regulation of living systems by electromagnetic cell-to-cell communication. Cellular membranes and DNA have been considered as possible sources of coherent excitations and photons, which may be involved in electromagnetic cell-to-cell communication (Frohlich 1968; Belyaev, Shcheglov et al. 1996; Belyaev, Alipov et al. 1998).

PD dependences of the MW effect at the 51.755 GHz resonance frequency were considerably different between two cell densities, $4 \cdot 10^7$ cells/ml and $4 \cdot 10^8$ cells/ml (Belyaev, Shcheglov et al. 1996). However, the resonance frequency of 51.755 GHz did not shift with the changes in cell density. The half-width of the 51.755 GHz resonance did not depend on cell density either. Contrary to the 51.755 GHz resonance response, the half-width of the 51.675 GHz resonance depended on cell density (Shcheglov, Belyaev et al. 1997). The data suggested that intracellular interaction during the NT MW exposures at some specific frequencies might affect sub-cellular targets for NT MW. This target is presumably chromosomal DNA that is organized in the DNA-domains (Belyaev, Alipov et al. 1992; Belyaev, Alipov et al. 1993; Matronchik and Belyaev 2005).

In all studies concerning dependence of the MW effects on cell density, the cells occupied a negligible part of the exposed volume and could not change the absorption of MW even at the highest cell densities (Belyaev, Alipov et al. 1994; Belyaev, Shcheglov et al. 1996; Shcheglov, Belyaev et al. 1997; Shcheglov, Alipov et al. 2002). Striking difference in the cell responses at various cell densities provided further evidence for non-thermal mechanism of the observed MW effects.

Significant MW effect on synchronization of *Saccharomyces carlsbergensis* yeast cells were observed by Golant and co-authors (Golant, Kuznetsov et al. 1994). Exposure to MW at 30 $\mu W/cm^2$ and 46 GHz induced synchronization as measured by cell density and bud formation. The authors assumed that MW induced cell-to-cell interaction resulting in the observed synchronization.

Possible role of intrinsic electromagnetic fields in cell-to-cell communication and mechanisms of their generation have recently been reviewed (Cifra, Fields et al. 2011).

XIII. GENETIC BACKGROUND AND CELL TYPE

Belyaev et al. have studied effects of MW on *E. coli* cells of three isogenic strains with different length of chromosomal DNA (Belyaev, Alipov et al. 1993). Bacterial chromosomal DNA in the cells of N99 wild type stain was lengthened by inserting DNA from λ and λ*imm*^{434}*bio*^{10} phages. Two strains were obtained with increased length of chromosomal DNA, N99(λ) and N99(λ,λ*imm*^{434}*bio*^{10}). The cells of these 3 strains were exposed to MW 10^{-10} at W/cm^2 and 10-17 frequencies within the ranges of 41.24-41.37 GHz and 51.69-51.795 GHz. The changes in chromatin conformation were analyzed before and after exposure. Clear resonance responses to MW were observed for each strain in both frequency ranges. However, each strain had its own resonance frequency, which were statistically significantly different between strains. All resonances had the same amplitude and half-width (Belyaev, Alipov et al. 1993). In each frequency band, all 3 resonances had the same effective circular polarization: right-handed in the 41.24-41.37 GHz band and left-handed within 51.69-51.795 GHz. All these data have led to conclusion that lengthening of chromosomal DNA resulted in shifting the resonance MW spectra of action. Importantly, these shifts in resonance frequencies could not be explained by the genetic activity of the inserted DNA. On the other hand, theoretical consideration based on oscillations of the DNA-domains regarding a whole nucleoid provided a good correlation between the increasing in the DNA length and the shifts in resonances (Belyaev, Alipov et al. 1993). A detailed analysis of MW effects on the cells of another *E. coli* strain, AB1157, at 10^{-10} W/cm^2 and various frequencies within 51.69-51.795 GHz, revealed the resonance frequency of 51.755$\pm$0.001 GHz (Belyaev, Shcheglov et al. 1996). This value was statistically significantly different from the resonance frequency of 51.765$\pm$0.002 in response of *E. coli* N99 cells to MW in the same frequency range (Belyaev, Shcheglov et al. 1996). It should be noted that both strains, AB1157 and N99, are considered as wild type strains. Nevertheless, these strains are different in their genotypes by several gene markers (Lukashevsky and Belyaev 1990; Belyaev, Alipov et al. 1992). These data provided evidence that cells of different origin, even being considered as wild type cells, might have different resonance responses to NT MW because of differences in their genotypes.

Stagg with colleagues exposed tissue cultures of transformed and normal rat glial cells to modulated MW (TDMA that conforms to the North American digital cellular telephone standard) at 836.55 MHz (Stagg, Thomas et al. 1997). Results from DNA synthesis assays differed for these two cell types. Sham-exposed and MW-exposed cultures of primary rat glial cells showed no significant differences for either log-phase or serum-starved condition. C6 glioma cells exposed to MW at 5.9

μW/g SAR (0.9 mW/cm^2) exhibited small (20-40 %) but significant increases in 38 % of [^{3}H]-thymidine incorporation experiments.

Repacholi with co-authors chronically exposed wild-type mice and E mu-Pim1 transgenic mice, which are moderately predisposed to develop lymphoma spontaneously, to plane-wave pulse-modulated MW at 900 MHz with a pulse repetition frequency of 217 Hz and a pulse width of 0.6 ms (Repacholi, Basten et al. 1997). Incident power densities were 2.6-13 W/m^2 and SARs were 0.008-4.2 W/kg, averaging 0.13-1.4 W/kg. The lymphoma risk was found to be significantly higher in the exposed transgenic mice. No effects were seen in the wild type mice.

Markkanen with colleagues found that MW affected the UV-induced apoptosis in *Saccharomyces cerevisiae* yeast cells KFy437 (cdc48-mutant) but did not modify apoptosis in KFy417 (wild-type) cells (Markkanen, Penttinen et al. 2004).

Czyz with colleagues exposed pluripotent embryonic stem (ES) cells of wild-type and deficient for the tumor suppressor p53 to pulse modulated GSM MW at 1.71 GHz (Czyz, Guan et al. 2004). Two dominant GSM modulation schemes (GSM-217 and GSM-Talk), which generate temporal changes between GSM-Basic (active during talking phases) and GSM-DTX (discontinuous transmission, which is active during listening phases thus simulating a typical conversation), were applied to the cells at and below the ICNIRP safety standards, 2 and 1.5 W/kg . GSM-217 MW induced a significant upregulation of mRNA levels of the heat shock protein hsp70 of p53-deficient ES cells differentiating in vitro, paralleled by a low and transient increase of c-jun, c-myc, and p21 levels in p53-deficient, but not in wild-type cells. Theses data further substantiated the notion that the genetic background determines cellular responses to GSM MW.

Nylund and Leszczynski have examined cell response to MW (900 MHz GSM-like signal, average SAR of 2.8 W/kg) using two human endothelial cell lines: EA.hy926 and EA.hy926v1 (Nylund and Leszczynski 2006). Gene expression changes were examined using cDNA Expression Arrays and protein expression changes were examined using 2-DE and PDQuest software. The same genes and proteins were differently affected by exposure in each of the cell lines.

Remondini et al. analyzed changes in gene expression in six human cell lines by gene microarrays (Remondini, Nylund et al. 2006). Cells were exposed to MW at 900 MHz GSM Basic mode, SAR 1.8-2.5 W/kg, 1 h exposure. Most cell lines responded to GSM-900 MHz, except for the CHME5 human microglial cells.

Rat1 and HeLa human cells were subjected to RF exposure at a frequency of 875 MHz with an intensity of 0.07 mW/cm2 (Friedman, Kraus et al. 2007). In Rat1 cells, phosphorylation peaked at 15 min after irradiation and returned to basal level within 30 min, whereas, in HeLa cells, peak phosphorylation was at 5 min after stimulation and decreased thereafter. Increases in Hb-

EGF release upon mobile phone irradiation were detected in both Rat1 and HeLa cell lines, although the amount released from irradiated HeLa cells was much higher than that released from Rat1 cells.

Zhao et al. studied whether expression of genes related to cell death pathways are dysregulated in primary cultured neurons and astrocytes by exposure to MW from GSM cell phone at the frequency of 1900 MHz for 2 h (Zhao, Zou et al. 2007). Microarray analysis and real-time RT-PCR have shown up-regulation of caspase-2, caspase-6 and Asc (apoptosis associated speck-like protein containing a card) gene expression in neurons and astrocytes. Up-regulation occurred in both "on" and "stand-by" modes in neurons, but only in "on" mode in astrocytes. Additionally, astrocytes showed up-regulation of the Bax gene. The authors concluded that even relatively short-term exposure to the cell phone radiation can up-regulate elements of apoptotic pathways in cells derived from the brain, and that neurons appear to be more sensitive to this effect than astrocytes.

Hoyto et al. analyzed the effects of MW exposure on cellular ornithine decarboxylase (ODC) activity in fibroblasts, two neural cell lines and primary astrocytes (Hoyto, Juutilainen et al. 2007). Several exposure times and exposure levels were used, and the fields were either unmodulated or GSM-like-modulated. Murine L929 fibroblasts, rat C6 glioblastoma cells, human SH-SY5Y neuroblastoma cells, and rat primary astrocytes were exposed to RF radiation at 872 MHz in a waveguide exposure chamber equipped with water cooling. Cells were exposed for 2, 8, or 24 hours to CW MW or to a GSM type signal pulse modulated at 217 Hz. ODC activity in rat primary astrocytes was decreased statistically significantly and consistently in all experiments performed at two exposure levels (1.5 and 6.0 W/kg) and using GSM modulated or CW radiation. In the secondary cell lines, ODC activity was generally not affected. The authors concluded that ODC activity was affected by MW exposure in rat primary neural cells, but the secondary cells used in this study showed essentially no response. In further studies by the same group, the difference in response of human SH-SY5Y neuroblastoma and mouse L929 fibroblast cells to a GSM-modulated MW at 872 MHz was replicated (Hoyto, Luukkonen et al. 2008).

Human cultured fibroblasts of three different donors and three different short-term human lymphocyte cultures were exposed to UMTS-like MW at 1950 MHz and the SAR below safety limit of 2 W/kg by Schwarz et al. (Schwarz, Kratochvil et al. 2008). The alkaline comet assay and the micronucleus assay were used to analyze genotoxic effects. UMTS exposure increased the comet tail factor (CTF) and induced centromere-negative micronuclei in human cultured fibroblasts in a dose and time-dependent way. No UMTS effect was obtained with lymphocytes, either unstimulated or stimulated with phytohemagglutinin. The authors concluded that UMTS exposure may cause genetic alterations in some but not in all human cells in vitro.

Del Vecchio et al. have tested viability, proliferation, and vulnerability of neural cells, after continuous radiofrequency (RF) electromagnetic fields exposure (global system for mobile telecommunications (GSM) modulated 900 MHz signal at a specific absorption rate (SAR) of 1 W/kg and maximum duration 144 h) generated by transverse electromagnetic cells. Two cellular systems, SN56 cholinergic cell line and rat primary cortical neurons were used (Del Vecchio, Giuliani et al. 2009). Exposure to RF did not change viability/proliferation rate of the SN56 cholinergic cells or viability of cortical neurons. Co-exposure to RF exacerbated neurotoxic effect of hydrogen peroxide in SN56, but not in primary cortical neurons, whereas no cooperative effects of RF with glutamate and 25-35AA beta-amyloid were found. These data suggest that only under particular circumstances (cell type and type of co-exposure) exposure to GSM modulated, 900MHz signal act as a co-stressor for oxidative damage of neural cells.

Gerner et al. exposed four different human cell types exposed to modulated GSM 1800 MHz at 2 W/kg (Gerner, Haudek et al. 2010). While short-term exposure did not significantly alter the proteome, an 8-h exposure caused a significant increase in protein synthesis in Jurkat T-cells and human fibroblasts, and to a lesser extent in activated primary human mononuclear cells (Gerner, Haudek et al. 2010). Quiescent (metabolically inactive) mononuclear white blood cells, did not detectably respond to GSM 1800 MHz. Most of the proteins found to be induced were chaperones, which are mediators of protein folding. Heat-induced proteome alterations detectable with used proteome methodology would require heating greater than 1°C. Because GSM-induced heating was less than 0.15°C, a heat-related response was excluded.

Dragicevic et al. evaluated brain mitochondrial function in aged Tg mice and non-transgenic (NT) littermates following 1 month of daily exposure to EMF at 918 MHz frequency, involved modulation with Gaussian minimal-shift keying (GMSK) signal, and SAR levels that varied between 0.25 and 1.05 W/kg (Dragicevic, Bradshaw et al. 2011).The cognitively-important brain areas of cerebral cortex and hippocampus in EMF-exposed mice exhibited clear increases in maximum mitochondrial respiration, while the striatum and amgydala were unaffected. For Tg mice, long-term EMF treatment induced a dramatic reduction in mitochondrial ROS levels in both cerebral cortex and hippocampus, but not in striatum or amygdala. By contrast, NT mice given EMF treatment did not show significant changes in ROS levels within any of the four brain areas analyzed. Therefore, EMF treatment reduced ROS levels selectively in Tg mice and selectively in cognitively-important brain areas.

Finally, it follows from the emerging data that MW effects are dependent on genotype and cell-type. These dependences may explain, at least partly, the discrepancies among studies from

different laboratories and demand careful selection of biological objects in designing the replication studies.

XIV. SEX-AND AGE-RELATED DIFFERENCES

There are few studies consistently indicating that MW may exert a sex-related influence on brain activity.

Papageorgiou and co-authors investigated the sex-related influence of MW similar to that emitted by GSM900 mobile phones on brain activity (Papageorgiou, Nanou et al. 2004). Baseline EEG energy of males was greater than that of females, and exposure to MW decreased EEG energy of males and increased that of females. Memory performance was invariant to MW exposure and sex influences.

Smythe and Costall reported the effects of mobile phone exposure on short- and long-term memory in male and female subjects (Smythe and Costall 2003). The results showed that males exposed to an active phone made fewer spatial errors than those exposed to an inactive phone condition, while females were largely unaffected. These results further indicated that mobile phone exposure has functional consequences for human subjects, and these effects appear to be sex-dependent.

Nam and colleagues exposed volunteers of both sex to MW emitted by a CDMA cellular phone for half an hour (Nam, Kim et al. 2006). Physiological parameters such as systolic and diastolic blood pressures, heart rate, respiration rate, and skin resistance were simultaneously measured. All the parameters for both groups were unaffected during the exposure except for decreased skin resistance of the male subjects (Nam, Kim et al. 2006).

Güler et al. exposed infant female and male white rabbits to 1800 MHz GSM like RF signal at SAR of 1.8 W/kg for 15 min/day during 7-14 days (Guler, Tomruk et al. 2012). Lipid peroxidation levels in the liver tissues of female and male infant rabbits increased under RF radiation exposure. Liver 8-hydroxy-2 ’-deoxyguanosine (8-OHdG) levels of female rabbits exposed to RF radiation were also found to increase when compared with the levels of non-exposed infants. However, there were no changes in liver 8-OHdG levels of male rabbits under RF exposure.

Santini et al. have performed a survey study on symptoms experienced during use of digital cellular phones using questionnaire of 161 students and workers in a French engineering school (Santini, Seigne et al. 2001). A significant increase in concentration difficult ($p < 0.05$) was reported by users of 1800-MHz (DCS) cellular phones compared to 900-MHz (GSM) phone users.

In users of cellular phones, women significantly ($p < 0.05$) complained more often of sleep disturbance than men. This sex difference for sleep complaint was not observed between women and men non-users of cellular phone. The use of both cellular phones and VDT significantly increased concentration difficulty. Digital cellular phone users also significantly ($p < 0.05$) more often complained of discomfort, warmth, and picking on the ear during phone conversation in relation with calling duration per day and number of calls per day. The complaint warmth on the ear might be a signal to users for stopping the call.

Prevalence of women (usually around 70%) among subjects, which report hypersensitivity to electromagnetic fields of wide frequency range including MW, may also provide indirect evidence for the gender-dependent effects of MW.

In his pioneering study concerning age in cancer risk from MW exposure, Hardell and colleagues found that the highest risks were associated with >5-year latency period in the youngest age group studied, 20-29-year, for analog phones (OR = 8.17, 95% CI = 0.94-71), and cordless phones (OR = 4.30, 95% CI = 1.22-15) (Hardell, Mild et al. 2004). Of note, no participants of age less 20 years were involved on this study. In further studies from the Hardell's group, highest risk was found in the age group <20 years at time of first use of wireless phones (Hardell and Carlberg 2009; Hardell, Carlberg et al. 2009).

Nam with co-authors reported that skin resistance in teenagers decreased by exposure to CDMA MW from cellular phones whereas no effects were seen in adults (Nam, Kim et al. 2006).

Capri et al. analyzed CD25, CD95, CD28 molecules in unstimulated and stimulated CD4+ e CD8+ T cells in vitro (Capri, Salvioli et al. 2006). Peripheral blood mononuclear cells (PBMCs) from young and elderly donors were exposed or sham-exposed to RF (1,800 MHz, SAR 2 W/kg) with or without mitogenic stimulation. No significant changes in the percentage of these cell subsets were found between exposed and sham-exposed lymphocytes in both young and elderly donors. Nevertheless, RF exposure induced a slight, but significant, downregulation of CD95 expression in stimulated CD4+ T lymphocytes from elderly, but not from young donors. This age-related result is noteworthy given the importance of such molecule in regulation of the immune response.

XV. INDIVIDUAL TRAITS

Shckorbatov et al. investigated electrokinetic properties of cell nuclei and condensation of heterochromatin in human buccal epithelium cells in response to MW at 42.2 GHz (Shckorbatov,

Grigoryeva et al. 1998). MW exposure decreased electric charge of cell nuclei and an increased chromatin condensation in dependence on individual traits of donors.

Individual variability in effects of GSM and UMTS MW on chromatin conformation and 53BP1/γ-H2AX DNA repair foci was observed in studies with lymphocytes from hypersensitive to EMF subjects and healthy persons (Sarimov, Malmgren et al. 2004; Belyaev, Hillert et al. 2005; Markova, Hillert et al. 2005; Belyaev, Markova et al. 2009). The same individual variability was reported for response of chromatin condensation human lymphocytes to ELF magnetic fields (Sarimov, Alipov et al. 2011). This variability correlated with initial state of chromatin in the exposed cells (Sarimov, Alipov et al. 2011). Thus, the data from two different research groups have indicated that the NT MW effects on human cells depended on initial sate of chromatin that individually varied between subjects.

Zotti-Martelli with colleagues exposed peripheral blood lymphocytes from nine different healthy donors for 60, 120 and 180 min to CW MW with a frequency of 1800 MHz and PD of 5, 10, and 20 mW/cm^2 and analyzed DNA damage using micronucleus (MN) assay (Zotti-Martelli, Peccatori et al. 2005). Both spontaneous and induced MN frequencies varied in a highly significant way among donors, and a statistically significant increase of MN, although rather low, was observed dependent on exposure time and PD. The data analysis highlighted a wide inter-individual and reproducible variability in the response.

Hinrikus et al. (Hinrikus, Bachmann et al. 2008) evaluated the effects of pulse-modulated MW (450 MHz) on human EEG rhythms. Thirteen healthy volunteers were exposed to MW; the field power density at the scalp was 0.16 m W/cm^2. Differences were found in individual sensitivity to exposure. Increases in the EEG beta power appeared statistically significant in the case of four subjects. In other study, the same authors confirmed and extended their observations on individual sensitivity to exposure with pulse-modulated MW. The experiments were carried out on four different groups of healthy volunteers. A 450-MHz MW modulated at 7 Hz (first group), 14 and 21 Hz (second group), 40 and 70 Hz (third group), 217 and 1000 Hz (fourth group) frequencies was applied. MW exposure, SAR 0.303 W/kg, increased the EEG energy. The proportion of subjects significantly affected was similar in all groups except for the 1000 Hz group: in the first group 16% at 7 Hz modulation; in the second group 31% at 14 Hz modulation and 23% at 21 Hz modulation; in the third group 20% at 40 Hz and 13% at 70 Hz modulation; in the fourth group 16% at 217 Hz and 0% at 1000 Hz modulation frequency.

Sannino et al. evaluated the induction of micronuclei in response to MW (900 MHz, average SAR of 1.25 W/kg) exposure and subsequent treatment with mitomycin C in peripheral blood lymphocytes from five human volunteers (Sannino, Sarti et al. 2009). MW exposure reduced the

level of mitomycin C –induced micronuclei in cells collected from four donors (i.e., responders). However, the effect of MW was not observed in the remaining donor (i.e., non-responder). The overall data indicated the existence of heterogeneity in the MW response among individuals.

Human sensitivity to radio frequency (RF) standing waves was tested using a movable reflecting wall (Huttunen, Hanninen et al. 2009). When the reflector was moved, the position of the maximums of the standing waves changed and the electromagnetic intensity changed in the body of the standing test subject. The computer with an AD-converter registered the signals of the hand movement transducer and the RF-meter with 100MHz dipole antennas. A total of 29 adults of different ages were tested. There were 9 persons whose hand movement graphs included features like the RF-meter. Six showed responses that did not correlate with the RF-meter. There were also 14 persons who did not react at all. Sensitive persons seem to react to crossing standing waves of the RF signals.

To conclude, while only few studies were performed, to evaluate individual sensitivity, the obtained results indicate dependence of response to MW exposure on individual traits.

XVI. PHYSIOLOGICAL VARIABLES: STAGE OF CELL GROWTH, TEMPERATURE, OXYGEN, DIVALENT METALS

The importance of physiological variables, which may include all conditions of cell culture growth such as aeration, the composition of the growth and exposure media, on NT MW effects has previously been reviewed (Grundler, Jentzsch et al. 1988). Since that time, significant body of new data has been accumulated unequivocally supporting the role of physiological variables for the NT MW effects, which should be carefully taken into account when replicating the original studies.

Belyaev et al. have reported that both value and direction of the MW effects strongly depended on the phase of culture growth, at which *E. coli* cells were exposed to CP or LP MW (100 $\mu W/cm^2$) at the resonance frequencies of 41.32 GHz and 51.76 GHz (Belyaev, Shcheglov et al. 1993; Belyaev, Alipov et al. 1994). At logarithmic phase of growth, MW resulted in condensation of nucleoids. In contrast, MW exposure decondensed nucleoids in cells if exposure was performed at the stationary phase of growth. It is known, that the state of nucleoid condensation depends on cell activity. In stationary cells nucleoids are more condensed compared to logarithmic cells that divide actively. It was concluded that MW are able to either stimulate or inhibit activity of the cells in dependence on stage of growth, stationary or logarithmic, respectively. Higher variability in effects was observed for logarithmic phase and effects were more stable for the stationary phase

that is characterized by partial synchronization of cells (Belyaev, Shcheglov et al. 1993; Belyaev, Alipov et al. 1994). There was no effect at all if cells were exposed at the end of the logarithmic phase where the MW effects changed their direction from inhibition to stimulation (Belyaev, Alipov et al. 1994). Another peculiarity was observed at the very beginning of the logarithmic stage, where the condensation of chromatin induced by MW was relatively weak. The AVTD data were confirmed by the electrophoretic analysis of proteins bound to DNA (Belyaev, Shcheglov et al. 1993). The effect in the stationary phase was characterized by a decrease in the quantity of several DNA-bound proteins with molecular weights of 61, 59, 56, 26, and 15 kDa. In contrast, abundance of some DNA-bound proteins, 61, 56, 51 and 43 kDa increased after exposure at the logarithmic phase. The decrease or increase in the abundance of DNA-bound proteins correlated with the observed changes in the state of nucleoids, decondensation or condensation, respectively.

Shcheglov et al. have studied effects of MW at the PD range of 10^{-18} to $3 \cdot 10^{-3}$ W/cm^2 stationary on logarithmic and stationary cells at various cell densities (Shcheglov, Alipov et al. 2002). Relatively weak response to MW was observed in exponentially growing cells. Partially synchronized stationary cells were more sensitive, especially at the cell densities above 10^8 cell/ml. The data suggested that the co-operative responses of cells to MW vary in dependence on phase of growth.

Recent data by Ushakov and colleagues indicated that the MW effects on *E. coli* cells depended on concentration of oxygen in the cell suspension during exposure (Ushakov, Alipov et al. 2005). This dependence might suggest that oxygen concentration should be indicated in order to improve reproducibility in replication studies.

Biological systems have been shown to be very sensitive to perturbations at conditions where critical components are at phase transition points, governed by local temperature, ionic strength and pH. This phenomenon was demonstrated by independent laboratories using 2.45-GHz MW radiation associated with a phase transition in lipid-protein complexes around 20-25 ^{0}C (Olcerst, Belman et al. 1980; Fisher, Poznansky et al. 1982; Liburdy and Vanek 1985; Allis and Sinha-Robinson 1987; Liburdy and Vanek 1987).

Fisher et al. have reported an effect of low-level 2450-MHz MW on total and ouabain-sensitive $24Na^+$ flux from human erythrocytes. Erythrocytes washed and loaded with $24Na^+$ were exposed at an absorption rate of 2.0-3.0 mW/ml suspension in a waveguide system under temperature- controlled conditions for 1 or 2 hr. Experiments were run in parallel, with exposed and sham- irradiated (control) samples, at various temperatures between 7 and 35^{0}C. Continuous-wave electromagnetic radiation at 2450 MHz had a significant effect on $24Na^+$ efflux, but only in the temperature range 22-25^{0}C. Total efflux increased an average of 23%; this was the result of an

increase in the ouabain-insensitive component (mean, 33%) and a decrease in the ouabain- sensitive portion (mean, 18%). These results indicated increased passive Na+ efflux and decreased ATPase-mediated Na+ efflux in erythrocytes exposed to low-level microwaves at 22-25^{0}C (Fisher, Poznansky et al. 1982).

Liburdy and Vanek have shown that MW-induced protein shedding is oxygen and temperature dependent (Liburdy and Vanek 1987). Microwaves (2450 MHz, 60 mW/g) resulted in the release or shedding of at least 11 low-molecular-weight proteins (<31,000 Da) from rabbit erythrocytes maintained in physiological buffer. This release was oxygen dependent and occured in 30 min for exposures conducted within the special temperature region of 17-21^{0}C, which is linked to a structural or conformational transition in the cell membrane. Shedding of 26,000 and 24,000 Da proteins was unique to MW treatment, with enhanced release of 28,000 and < 15,000 Da species upon MW exposure. Two-dimensional isoelectric focusing revealed that proteins of< 14,000 Da shed during microwave treatment exhibited a pI of 6.8-7.3 not seen in sham-treated cells. When erythrocytes were maintained at 17-21^{0}C in the absence of divalent cations, release of 28,000-31,000 and < 14,000 Da components was detected. This indicated that cation-bridge stability may be important for release of these proteins. The results provided evidence that MW alter erythrocyte protein composition at temperatures linked to a transition in the cell membrane and that destabilization of salt bridges may play a role in an interaction mechanism for protein release (Liburdy and Vanek 1987).

The ATPase activity in human red blood cell membranes was investigated in vitro as a function of temperature and exposure to 2,450-MHz continuous wave microwave radiation to confirm and extend a report of Na^+ transport inhibition under certain conditions of temperature and exposure (Allis and Sinha-Robinson 1987). Assays were conducted spectrophotometrically during microwave exposure with a custom-made spectrophotometer-waveguide apparatus. Temperature profiles of total ATPase and Ca^{+2} ATPase (ouabain-inhibited) activity between 17 and 31 degrees C were graphed as an Arrhenius plot. Each data set was fitted to two straight lines which intersect between 23 and 24 degrees C. The difference between the total and Ca^{+2} ATPase activities, which represented the Na^+/K^+ ATPase activity, was also plotted and treated similarly to yield an intersection near 25 degrees C. Exposure of membrane suspensions to electromagnetic radiation, at a dose rate of 6 W/kg and at five temperatures between 23 and 27 degrees C, resulted in an activity change only for the Na^+/K^+ ATPase at 25 degrees C. The activity decreased by approximately 35% compared to sham-irradiated samples. A possible explanation for the unusual temperature/microwave interaction was proposed (Allis and Sinha-Robinson 1987).

Therefore, temperature may be an important variable, which should be taken into account while analyzing response of cells to MW.

Similar to the effects of ELF (Belyaev, Alipov et al. 1999), the MW effects were reported to be dependent on concentration of divalent ions (Gapeev, Iakushina et al. 1997).

In conclusion, physiological parameters such as stage of cell growth, temperature, oxygen an divalent ions temperature may be an important variable, which should be taken into account while analyzing response of cells to MW.

XVII. ANTIOXIDANTS AND RADICAL SCAVENGERS

Oxidative stress caused by biological, chemical and physical factors has been associated with increased risk of human cancer at various sites. Human cells induce and/or activate several oxidant generating enzymes that produce high concentrations of diverse free radicals and oxidants. These reactive species can damage DNA, RNA, lipids and proteins, leading to increased mutations and altered function of enzymes and proteins, thus contributing to the multistage carcinogenesis process. Control of oxidative stress is being explored as an approach to chemoprevention of human cancers (IARC 2002).

It is well known that endogenous (intracellular) free radicals, which are collectively called reactive oxygen species (ROS), arise from mitochondrial oxidative metabolism and other reactions in cells (Pollycove and Feinendegen 2003). The estimated average generation rate is $\sim 10^9$ ROS per cell per day (Beckman and Ames 1998), which results in 10^6 oxidative DNA damage, 10^5 SSBs and 0.1 DSBs per cell per day (Pollycove and Feinendegen 2003).

In their pioneering study, Lai and Singh described the effects of MW on the rat brain cells as measured using a microgel electrophoresis assay (Lai and Singh 1996). These effects were significantly blocked by treatment of rats either with the spin-trap compound N-tert-butyl-α-phenylnitrone or with melatonin, both agents being free radical scavengers and antioxidants (Lai and Singh 1997). These data suggested that free radicals might be involved in the effects of MW. The ability of scavengers and antioxidants has been tested by many other research groups an in all cases, this treatment inhibiter the reported TN MW effects.

Oktem andcolleagues exposed rats to MW from GSM900 mobile phone with and without melatonin treatment (Oktem, Ozguner et al. 2005). Malondialdehyde (MDA), an index of lipid peroxidation, and urine N-acetyl-beta-d-glucosaminidase (NAG), a marker of renal tubular damage, were used as markers of oxidative stress-induced renal impairment. Superoxide dismutase (SOD),

catalase (CAT), and glutathione peroxidase (GSH-Px) activities were studied to evaluate changes in antioxidant status. In the MW-exposed group, while tissue MDA and urine NAG levels increased, SOD, CAT, and GSH-Px activities were reduced. Melatonin treatment inhibited these effects. The authors concluded that melatonin might exhibit a protective effect on mobile phone-induced renal impairment in rats.

Ozguner and colleagues exposed Wistar-Albino rats to MW from GSM900 mobile phone with and without melatonin and analyzed histopathologic changes in skin (Ozguner, Aydin et al. 2004). MW induced increase in thickness of stratum corneum, atrophy of epidermis, papillamatosis, basal cell proliferation, granular cell layer (hypergranulosis) in epidermis and capillary proliferation. Impairment in collagen tissue distribution and separation of collagen bundles in dermis were all observed in exposed animals as compared to the control group. Most of these changes, except hypergranulosis, were prevented with melatonin treatment. The authors concluded that exposure to GSM900 MW caused mild skin changes and melatonin treatment could reduce these changes. In other studies of the same group, the ability of melatonin to reduce various MW-induced effects was confirmed and inhibitory potential of the antioxidant caffeic acid phenethyl ester (CAPE) was reported (Ozguner, Altinbas et al. 2005; Ozguner, Oktem et al. 2005; Ozguner, Oktem et al. 2005; Ozguner, Bardak et al. 2006).

Ayata et al. analyzed the effects of 900 MHz MW with and without melatonin on fibrosis, lipid peroxidation, and anti-oxidant enzymes in rat skin (Ayata, Mollaoglu et al. 2004). The levels of MDA and hydroxypyroline and the activities of SOD, GSH-Px, and CAT were studied. MDA and hydroxyproline levels and activities of CAT and GSH-Px were increased significantly in the exposed group without melatonin and decreased significantly in the exposed group with melatonin. SOD activity was decreased significantly in the exposed group and this decrease was not prevented by the melatonin treatment. The authors assumed that the rats irradiated with MW suffer from increased fibrosis and lipid peroxidation and that melatonin can reduce the fibrosis and lipid peroxidation caused by MW.

Ilhan with co-authors investigated oxidative damage in brain tissue of rats exposed to GSM900 MW with and without pretreatment with Ginkgo biloba (Gb) (Ilhan, Gurel et al. 2004). MW induced oxidative damage measured as: (i) increase in MDA and nitric oxide (NO) levels in brain tissue, (ii) decrease in brain SOD and GSH-Px activities, and (iii) increase in brain xanthine oxidase and adenosine deaminase activities. These MW effects were prevented by the Gb treatment. Furthermore, Gb prevented the MW-induced cellular injury in brain tissue revealed histopathologically. The authors concluded that reactive oxygen species may play a role in the

adverse effects of GSM900 MW and Gb prevents the MW-induced oxidative stress by affecting antioxidant enzymes activity in brain tissue.

Guney et al.examined 900 MHz mobile phone-induced oxidative stress that promotes production of ROS and investigated the role of vitamins E and C, which have antioxidant properties, on endometrial tissue against possible 900 MHz mobile phone-induced endometrial impairment in rats (Guney, Ozguner et al. 2007). The animals were randomly grouped (eight each) as follows: 1) Control group (without stress and EMR, Group I), 2) sham-operated rats stayed without exposure to EMR (exposure device off, Group II), 3) rats exposed to 900 MHz EMR (EMR group, Group III) and 4) a 900 MHz EMR exposed + vitamin-treated group (EMR + Vit group, Group IV). A 900 MHz EMR was applied to EMR and EMR + Vit group 30 min/day, for 30 days. Endometrial levels of nitric oxide (NO, an oxidant product) and malondialdehyde (MDA, an index of lipid peroxidation), increased in EMR exposed rats while the combined vitamins E and C caused a significant reduction in the levels of NO and MDA. Likewise, endometrial superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px) activities decreased in EMR exposed animals while vitamins E and C caused a significant increase in the activities of these antioxidant enzymes. In the EMR group histopathologic changes in endometrium, diffuse and severe apoptosis was present in the endometrial surface epithelial and glandular cells and the stromal cells. Diffuse eosinophilic leucocyte and lymphocyte infiltration were observed in the endometrial stroma whereas the combination of vitamins E and C caused a significant decrease in these effects of EMR. It is concluded that oxidative endometrial damage plays an important role in the 900 MHz mobile phone-induced endometrial impairment and the modulation of oxidative stress with vitamins E and C reduces the 900 MHz mobile phone-induced endometrial damage both at biochemical and histological levels.

Koylu et al. studied the effects of MW on the brain lipid peroxidation in rats, and the possible protective effects of melatonin on brain degeneration induced by MW (Koylu, Mollaoglu et al. 2006). The levels of lipid peroxidation in the brain cortex and hippocampus increased in the MW group compared with the control group, although the levels in the hippocampus were decreased by combined administration of MW and melatonin. Brain cortex lipid peroxidation levels were unaffected by melatonin treatment. The authors concluded that melatonin may prevent MW-induced oxidative stress in the hippocampus by strengthening the antioxidant defense system.

Balci et all exposed albino Wistar rats to mobile-phone-emitted radiation and analyzed oxidant/antioxidant balance in corneal and lens tissues. The results of this study suggest that mobile telephone radiation leads to oxidative stress in corneal and lens tissues and that antioxidants such as vitamin C can help to prevent these effects (Balci, Devrim et al. 2007).

Sokolovic et al. evaluated the intensity of oxidative stress in the brain of Wistar rats chronically exposed to MW from mobile phones (SAR = 0.043-0.135 W/kg) during 20, 40 and 60 days (Sokolovic, Djindjic et al. 2008). A significant increase in brain tissue malondialdehyde (MDA) and carbonyl group concentration was found. Decreased activity of catalase (CAT) and increased activity of xanthine oxidase (XO) remained after 40 and 60 days of MW exposure. Melatonin treatment significantly prevented the increases in MDA content and XO activity in the brain tissue after 40 days of exposure while it was unable to prevent the decrease of CAT activity and increase of carbonyl group contents. The authors concluded that exposure to the mobile phone MW caused oxidative damage in the brain and that treatment with melatonin significantly prevented this oxidative damage.

Gajski and Garaj-Vrhovac investigated the radioprotective effect of bee venom against DNA damage induced by 915-MHz microwave radiation (SAR of 0.6 W/kg) (Gajski and Garaj-Vrhovac 2009). Whole blood lymphocytes of Wistar rats are treated with 1 mg/mL bee venom 4 hours prior to and immediately before irradiation. Standard and formamidopyrimidine-DNA glycosylase (Fpg)–modified comet assays were used to assess basal and oxidative DNA damage produced by ROS. Bee venom decreased basal and oxidative DNA damage induced by microwave radiation. The difference between the comet assay results in the presence and in the absence of Fpg-enzyme suggested that oxidative stress is responsible for the DNA damage induced by microwave radiation. Among other possible mechanisms, antioxidant activity of bee venom may likely account for the radioporotective effect.

Esmekaya et al. analyzed effects of 1.8 GHz GSM alone and in combination with Ginkgo biloba (EGb 761) pre-treatment in human peripheral blood lymphocytes (Esmekaya, Aytekin et al. 2011). RF exposure significantly increased frequency of sister chromatid exchanges (SCE) and inhibited cell viability. No temperature difference was observed between sham control and RF exposed cells, so the observed effects may be considered as non-thermal. EGb 761 pre-treatment significantly reduced both RF effects. The authors concluded that EGb 761 had a protective role against RF induced mutagenesis.

Ozgur et al investigated oxidative damage and antioxidant enzyme status in the liver of guinea pigs exposed to mobile phone-like radiofrequency radiation (RFR) and the potential protective effects of N-acetyl cysteine (NAC) and epigallocatechin-gallate (EGCG) on the oxidative damage (Ozgur, Gler et al. 2010). Nine groups of guinea pigs were used to study the effects of exposure to an 1800-MHz Global System for Mobile Communications (GSM)-modulated signal (average whole body Specific Absorption Rate (SAR) of 0.38W/kg, 10 or 20 min per day for seven days) and treatment with antioxidants. Significant increases in malondialdehyde (MDA) and total

nitric oxide (NO) levels and decreases in activities of superoxide dismutase (SOD), myeloperoxidase (MPO) and glutathione peroxidase (GSH-Px) were observed in the liver of guinea pigs after RFR exposure. NAC treatment induced increase in hepatic GSH-Px activities, whereas EGCG treatment alone attenuated MDA level. Extent of oxidative damage was found to be proportional to the duration of exposure. Authors concluded that the adverse effect of RFR may be related to the duration of mobile phone use. NAC and EGCG may protect the liver tissue against the RFR-induced oxidative damage and enhance antioxidant enzyme activities.

Female rats were exposed to a mobile phone signal (900 MHz), the mobile phone plus vitamin C group was exposed to a mobile phone signal (900 MHz) and treated orally with vitamin C (Imge, Kilicoglu et al. 2010). Malondialdehyde (MDA), antioxidant potential (AOP), superoxide dismutase, catalase (CAT), glutathione peroxidase (GSH-Px), xanthine oxidase, adenosine deaminase (ADA) and 5'nucleotidase (5'-NT) were analyzed in brain tissues. MW exposure caused an inhibition in 5'-NT and CAT activities. GSH-Px activity and the MDA level were also found to be reduced in the mobile phone group but not significantly. Vitamin C caused a significant increase in the activity of GSH-Px and non-significant increase in the activities of 5'-NT, ADA and CAT enzymes. The results suggest that vitamin C may play a protective role against detrimental effects of mobile phone radiation in brain tissue.

To conclude this section, several studies consistently show that supplementation with antioxidants and radical scavengers can reduce MW effects. In other words, the level of radicals should be considered as an important parameter for the NT MW effects. Moreover, these studies indicate that induction of radicals is one of the key events in bioeffeds of NT MW.

XVIII. CO-EXPOSURE

Zmyslony et al have studied effects of 930 MHz continuous wave (CW) electromagnetic field, 1.5 W/kg, on the reactive oxygen species (ROS) level in rat lymphocytes (Zmyslony, Politanski et al. 2004). Acute (5 and 15 min) exposure did not induce ROS. However, this exposure increased effect of $FeCl_2$, 10 μg/ml.

Co-exposure to RF (global system for mobile telecommunications (GSM) modulated 900MHz signal at a specific absorption rate (SAR) of 1 W/kg and maximum duration 144 h) exacerbated neurotoxic effect of hydrogen peroxide in SN56, but not in primary cortical neurons (Del Vecchio, Giuliani et al. 2009). These data suggest that only under particular circumstances

(cell type and type of co-exposure) exposure to GSM modulated, 900MHz signal act as a co-stressor for oxidative damage of neural cells.

XIX. REPLICATION STUDIES

Obviously, not taking into account the dependences of NT MW effects on a number of physical parameters and biological variables may result in misleading conclusions regarding the reproducibility of these effects. Especially important might be the observations that NT MW could inhibit or stimulate the same functions dependent on conditions of exposure (Pakhomov, Akyel et al. 1998). Under different conditions of exposure, MW either increased or decreased the growth rate of yeast cells (Grundler, Jentzsch et al. 1988), the radiation-induced damages in mice (Sevast'yanova 1981), the respiratory burst in neutrophils of mice (Gapeev, Iakushina et al. 1997), the condensation of nucleoids in *E coli* cells (Belyaev, Shcheglov et al. 1993; Belyaev, Alipov et al. 1994) and human lymphocytes (Sarimov, Malmgren et al. 2004). Potentially bi-directional effects of MW should be taken into account in replication studies.

In some cases when the conditions were kept in strict control, the effects we reproduced. Highly resonant effects of ultra-weak MW (near 70 GHz) on the induction of λ-phage were first established by Webb (Webb 1979), and subsequently corroborated (Lukashevsky and Belyaev 1990).

Despite of considerable body of studies with NT MW in biology, only a few studies were performed to independently replicate the original data on the NT MW effects. It should be noted, that these replications are usually not completely comparable with the original studies because of either missing description of important parameters of exposure or significant differences in these parameters between original study and replication. One well-known attempt to replicate the results of Gründler was the study by Gos and co-authors (Gos, Eicher et al. 1997). No MW effects were observed in this replication study. However, the deviations from the Gründler's protocol might be a simple reason for poor reproducibility. For example, synchronized cells were used in studies of Gründler. Contrary to the Gründler's original protocol, Gos used exponentially growing cells. If the MW effects in yeast cells are dependent on stage of growth, cell density and intercellular interactions as it has been described for *E. coli* cells (Belyaev, Shcheglov et al. 1993; Belyaev, Alipov et al. 1994; Belyaev, Shcheglov et al. 1996; Shcheglov, Belyaev et al. 1997), no response should be expected in the logarithmic phase of growth. Gos and colleagues used *S. cerevisiae* strain with the auxotrophy mutations for leucine and uracil. Gründler used the wild type strain. It might

suggest another cause for the deviations between the data of Gründler and Gos. Despite orientation of SMF in respect to electric and magnetic components of MW was the same, the values of SMF were different. The stray ELF field was 120 nT in the study by Gos, that is higher than usually observed background fields, < 50 nT. The spectral characteristics of the background fields, which were described only in the study by Gos, might be also different. In addition, the conditions of cell cultivation might vary between studies; for example, the data on oxygen concentration in media used in both studies are not available.

Lai and Singh have consistently reported that circularly polarized MW exposure at 2450 MHz induced DNA damage in brain cells of the exposed rats (Lai and Singh 1995; Lai and Singh 1996; Lai and Singh 1997). Replication studies have also tested circularly polarized MW exposure at 2450 MHz and no induced DNA damage was reported (Malyapa, Ahern et al. 1997; Malyapa, Ahern et al. 1998; Lagroye, Anane et al. 2004). All these replication studies have used another exposure system. However, handedness of circular polarization has not been given neither in original study, no in replications. If the handedness was different between studies it could reasonably account for inconsistency.

Most reviews of the experimental studies do not include analysis of various biological variables and physical parameters when comparing the data on the NT MW effects from different studies. As result, misleading conclusion is often made that MW at NT levels produce no "reproducible" effects.

XX. SIMILARITY OF MICROWAVE AND ELF EFFECTS

Mobile phones not only expose the user to RF EMF but also to ELF EMF (Linde and Mild 1997; Heath, Jenvey et al. 1998; Jokela, Puranen et al. 2004; Ilvonen, Sihvonen et al. 2005; Cook, Saucier et al. 2006; Perentos, Iskra et al. 2007). Perentos et al. have recently measured and characterized the ELF magnetic field from several commercial GSM handsets (the RF characteristics being already well understood) using different probes which covered frequency range from static magnetic fields ("0 Hz") to 2 GHz. Peak ELF fields at the front sides of 5 commercial GSM phones were assessed and a maximum of 22.4 μT was reported (Perentos, Iskra et al. 2008). The main ELF component at the 217 Hz was about 1 μT at the distance of 3 cm from the handset front side. The overall pulse peak was 4.2 times greater than the 217 Hz component. 217 Hz magnetic field decreased with distance and reached 0.3 μT approximately at 5 cm from the front handset side. The overall ELF pulse peak produced by all ELF components was 4.2 times greater

than the 217 Hz component. The ELF fields higher 0.3 μT have consistently been shown to correlate with increased risk of children leukemia in several studies covering European countries, USA and Japan (Kabuto, Nitta et al. 2006; Yang, Jin et al. 2008). Similar to RF, ELF has been classified by the IARC as possible carcinogen "2B". It has been known for long time that weak ELF fields and NT MW result to similar effects with significant overplaying of molecular biological pathways for their appearance (Adey 1981; Blank and Goodman 2009; Davanipour and Sobel 2009). Multiple data on ELF biological effects at intensities below the ICNIRP standards are available showing their complex dependence of the ELF effects on biological and physical variables (Belyaev, Alipov et al. 1999; Blank and Goodman 2009; Phillips, Singh et al. 2009; Sarimov, Alipov et al. 2011). In particular, stress response, molecular pathways for generation of reactive oxygen species (ROS), increased sensitivity of stem cells, and inhibition of melatonin production (Burch, Reif et al. 2000) were suggested as mechanisms which link observed increase in cancer risks and effects of exposure at the cellular level. EMF effects in a wide frequency range from ELF to MW have been considered in the frames of the same physical models (Chiabrera, Bianco et al. 1991; Matronchik, Alipov et al. 1996; Chiabrera, Bianco et al. 2000; Binhi 2002; Panagopoulos, Karabarbounis et al. 2002; Matronchik and Belyaev 2005; Matronchik and Belyaev 2008).

In many cases, because of ELF modulation and additional ELF fields created by the MW sources, for example by mobile phones, it is difficult to distinguish the effects of exposures to ELF and MW. Therefore, these combined exposures and their possible cancer risks should be considered in combination.

XXI. CANCER RISK ASSESSMENT FROM MECHANISTIC POINT OF VIEW

At present, a new situation has arisen when a significant part of the general population is exposed chronically (much longer than previously investigated durations of exposures) to NT MW from different types of mobile communication including GSM and UMTS/3G phones and base stations, WLAN (Wireless Local Area Networks), WPAN (Wireless Personal Area Networks such as Bluetooth), DECT (Digital Enhanced (former European) Cordless Telecommunications) wireless phones (Joseph, Frei et al. 2010). Multiple sources of mobile communication result in chronic exposure of general population to MW at the non-thermal levels. These exposures are characterized by low intensities, varieties and complexities of signals, and long-term durations of exposure that are comparable with a lifespan.

Most of the real signals that are in use in mobile communication have not been tested so far. Very little research has been done with real signals and for durations and intermittences of exposure that are relevant to chronic exposures from mobile communication. In some studies, so-called "mobile communication-like" signals were investigated that in fact were different from the real exposures in such important aspects as intensity, carrier frequency, modulation, polarization, duration and intermittence.

Emerging evidence suggests that the SAR concept, which has been widely adopted for safety standards, is not useful alone for the evaluation of health risks from NT MW of mobile communication. The role of other exposure parameters such as frequency, modulation, polarization, duration, and intermittence of exposure should be taken into account.

IARC has recently classified RF as a 'Possible Human Carcinogen' (Class 2B) (Baan, Grosse et al. 2011). Contrary to other panels, such as ICNIRP, whose members dismiss the NT MW effects based on their "non-reproducibility" and lack of comprehensive mechanisms, the IARC working group included scientists, which argued for existence of non-thermal effects and their complex dependence on variety of biological and physical parameters which should be included in consideration. By its classification, IARC has justified implementation of the Precautionary Principle, confirmed the existence of non-thermal effects that can cause health risks, and indicated that the current safety standards are insufficient to protect health.

The data about the effects of MW at super low intensities and significant role of duration of exposure in these effects along with the data showing that adverse effects of NT MW from GSM/UMTS mobile phones depend on carrier frequency and type of the MW signal suggest that MW from base-stations/masts, wireless routers, WI-FI and other wireless devices and exposures in common use today can also produce adverse effects at prolonged durations of exposure.

So far, most laboratory and epidemiological studies did not control important features of the NT MW effects and therefore, only limited conclusion regarding health effects of MW from mobile communication can be drawn from these studies. The group of Hardell was the first epidemiologic studying separately the MW signals from cordless phones, analogue phones and digital phones (Hardell, Hansson Mild et al. 2001; Hardell, Hansson Mild et al. 2003; Hardell, Eriksson et al. 2005; Hardell and Hansson Mild 2005). This approach is valid from the mechanistic point of view.

Nowadays, it is almost impossible to select control unexposed groups because the whole population in many countries is exposed to wide range of MW signals from various sources such as mobile phones, base stations/masts, WLAN, WPAN, DECT wireless phones and given that duration of exposure (at least 10 years for cancer latency period) is also important for the effects of NT MW along PD/SAR. Exposure from downlink sources (base stations *etc.*) may contribute up to

90% of total environmental outdoor-urban exposure in European countries while exposure to DECT phone is comparable to exposure to mobile phones (Frei, Mohler et al. 2009; Frei, Mohler et al. 2010; Joseph, Frei et al. 2010). In other words, there are no unexposed control groups available for epidemiologic studies in the developed countries. Substantial variation in relative ratio of downlink and uplink signals between countries (Joseph, Frei et al. 2010) can at least partially account for differences in epidemiologic data because of variation in exposure of control groups to downlink signals.

While several national registers (Norway, Australia, Finland, Denmark) report increased incidence of brain cancer, US and Swedish ones do not. This inconsistence may be accounted by deficit in reporting of tumors to the Swedish Cancer Registry (Hardell and Carlberg 2009).

Importantly, because the signals are completely replaced by other signals faster then once per 10 years, duration comparable with latent period, epidemiologic studies can not provide basement for assessment of upcoming new signals.

As far as different types of MW signals (carrier frequency, modulation, polarization, far and near field, intermittence, coherence, *etc.*) may produce different effects, cancer risks should ideally be estimated for each MW signal separately. In other words, one type of MW signal would correspond to one chemical compound. That means, for example, that each from 124 signals involved in GSM uplink mobile communication should be separately evaluated to fit situation accepted for estimation of cancer risks from chemical compounds.

It now appears that most, if not all, adult tissues and organs including blood and brain contain stem cells (Metcalfe and Ferguson 2008). Almost all hematopoietic and solid neoplasms arise from cancer stem cells that are dysfunctional versions of a normal stem cells. Current models for radiation carcinogenesis have paid much attention to the stochastic process of energy deposition in cells, but accumulating evidences have shown that the nature of the target cells, i.e. tissue stem cells and progenitor cells, needs to be taken into consideration (Niwa 2010; Richardson 2011). Stem cell self-renewal and progenitor differentiation is regulated by the specialized microenvironment—or "niche"—in which these cells reside (Alvarez-Buylla and Lim 2004) and which regulate stem cells (Morrison and Spradling 2008; Johansson, Cappello et al. 2010; Kim and Shivdasani 2012; Sugiyama and Nagasawa 2012)..Importance of stem cells for carcinogenesis, challenges the definition of volume for SAR determination in safety standards. Instead of random distribution of targets for carcinogenesis, localized distribution of SAR in stem cells and niches is needed. Because very small size of the niches in different tissues including the brain (Kazanis 2012), the SAR averaging should be performed at volumes much less then currently accepted 10 g. Decreasing the sensitive volume to the stem cell niches with sizes down to 10 μm (Richardson 2011) may likely

put almost all mobile phones out of the current safety standards, even given that they are only based on thermal effects and do not consider any other parameters except for SAR. From point view of stem cell organization, the volume of SAR determination may be especially important for setting the safety standards for children. During brain development, most stem cells and their niches are spatially ephemeral and temporally transient as the cellular and molecular "puzzle" behind neurogenesis and morphogenesis is "assembled" and "disassembled" at a dazzling pace. In contrast, in the adult, neural stem cells and their niches are retained in restricted regions with their local developmental processes occurring for the life (Alvarez-Buylla and Lim 2004).

It should be anticipated that some part of the human population, such as children, pregnant women and groups of hypersensitive persons could be especially sensitive to the NT MW exposures.

XXII. CONCLUSIONS

Non-thermal effects of microwaves depend on variety of biological and physical parameters that should be taken into account in setting the safety standards. These exposures can cause health risk. The current safety standards are insufficient to protect from non-thermal microwave effects. Emerging evidence suggests that the SAR concept, which has been widely adopted for safety standards, is not useful alone for the evaluation of health risks from NT MW of mobile communication. Other parameters of exposure, such as frequency, modulation, duration, dose should be taken into account. New standards should be developed based on knowledge of mechanisms of non-thermal effects. Importantly, because the signals of mobile communication are completely replaced by other signals faster then once per 10 years, duration comparable with latent period, epidemiologic studies cannot provide basement for cancer risk assessment from upcoming new signals. Precautionary Principle should be implemented while new standards are in progress. In many cases, because of ELF modulation and additional ELF fields created by the MW sources, for example by mobile phones, it is difficult to distinguish the effects of exposures to ELF and MW. Therefore, these combined exposures and their possible cancer risks should be considered in combination. It should be anticipated that some part of the human population, such as children, pregnant women and groups of hypersensitive persons could be especially sensitive to the non-thermal microwave exposures.

REFERENCES

Adang D, Remacle C, Vorst AV. 2009. Results of a long-term low-level microwave exposure of rats. IEEE Transactions on Microwave Theory and Techniques 57(10):2488-2497.

Adey WR. 1981. Tissue interactions with nonionizing electromagnetic fields. Physiological Reviews 61:435-514.

Adey WR. 1999. Cell and molecular biology associated with radiation fields of mobile telephones. Review of Radio Science 1996-1999, W R Stone and S Ueno Oxford, Oxford University Press:845-872.

Adey WR, Bawin SM, Lawrence AF. 1982. Effects of weak amplitude-modulated microwave fields on calcium efflux from awake cat cerebral cortex Bioelectromagnetics 3:295-307.

Agarwal A, Deepinder F, Sharma RK, Ranga G, Li J. 2008. Effect of cell phone usage on semen analysis in men attending infertility clinic:An observational study Fertility and Sterility 89:124-128.

Agarwal A, Desai NR, Makker K, Varghese A, Mouradi R, Sabanegh E, et al. 2009. Effects of radiofrequency electromagnetic waves .RF-EMW. from cellular phones on human ejaculated semen:an in vitro pilot study Fertility & Sterility 92:1318-1325.

Akoev IG, Pashovkina MS, Dolgacheva LP, Semenova TP, Kalmykov VL. 2002. [Enzymatic activity of some tissues and blood serum from animals and humans exposed to microwaves and hypothesis on the possible role of free radical processes in the nonlinear effects and modification of emotional behavior of animals] Radiatsionnaia Biologiia Radioecologiia 42:322-330.

Alipov ED, Shcheglov VS, Sarimov RM, Belyaev IY. 2003. Cell-density dependent effects of low-dose ionizing radiation on E coli cells. Radiatsionnaia Biologiia Radioecologiia 43:167-171.

Alipov YD, Belyaev IY, Kravchenko VG, Polunin VA, Shcheglov VS. 1993. Experimental justification for generality of resonant response of prokaryotic and eukaryotic cells to MM waves of super-low intensity. Physics of the Alive 1:72-80.

Allis JW, Sinha-Robinson BL. 1987. Temperature-specific inhibition of human red cell Na+/K+ ATPase by 2,450-MHz microwave radiation Bioelectromagnetics 8:203-212.

Alvarez-Buylla A, Lim DA. 2004. For the long run:maintaining germinal niches in the adult brain. Neuron 41:683-686.

Ayata A, Mollaoglu H, Yilmaz HR, Akturk O, Ozguner F, Altuntas I. 2004. Oxidative stress-mediated skin damage in an experimental mobile phone model can be prevented by melatonin. Journal of Dermatology 31:878-883.

Baan R, Grosse y, Lauby-Secretan b, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, et al. 2011. Carcinogenicity of radiofrequency electromagnetic fields Lancet Oncology 12:624-626.

Balci M, Devrim E, Durak I. 2007. Effects of mobile phones on oxidant/antioxidant balance in cornea and lens of rats. Current Eye Research 32:21-25.

Banik S, Bandyopadhyay s, Ganguly S. 2003. Bioeffects of microwave - a brief review. Bioresource Technology 87:155-159.

Bartsch H, Kupper H, Scheurlen U, Deerberg F, Seebald E, Dietz K, et al. 2010. Effect of chronic exposure to a GSM-like signal .mobile phone. on survival of female Sprague-Dawley rats:modulatory effects by month of birth and possibly stage of the solar cycle Neuro Endocrinology Letters 31:457-473.

Beckman KB, Ames BN. 1998. The free radical theory of aging matur. Physiological Reviews 78:547-581.

Belyaev I. 2010. Dependence of non-thermal biological effects of microwaves on physical and biological variables:implications for reproducibility and safety standards European Journal of Oncology - Library NON-THERMAL EFFECTS AND MECHANISMS OF INTERACTION BETWEEN ELECTROMAGNETIC FIELDS AND LIVING MATTER An ICEMS Monograph L Giuliani and M Soffritti Bologna, Italy, RAMAZZINI INSTITUTE, Vol 5:187-218. Available at:http://wwwicemseu/papershtm?f=/c/a/2009/12/15/MNHJ1B49KHDTL

Belyaev IY .1992. Some biophysical aspects of the genetic effects of low intensity millimeter waves. Bioelectrochemistry Bioenergetics 27:11-18.

Belyaev IY. 1993. Biological effects of low dose ionizing radiation and weak electromagnetic fields 7th Workshop on Microdosimetry S G Andreev Suzdal, MIFI Publisher:128-146.

Belyaev IY, Alipov ED. 2001. Frequency-dependent effects of ELF magnetic field on chromatin conformation in Escherichia coli cells and human lymphocytes. Biochimica et Biophysica Acta 1526:269-276.

Belyaev IY, Alipov ED, Harms-Ringdahl M. 1999. Effects of weak ELF on E coli cells and human lymphocytes:role of genetic, physiological and physical parameters. Electricity and Magnetism in Biology and Medicine F Bersani NY, Kluwer Academic:481-484.

Belyaev IY, Alipov YD, Harms-Ringdahl M. 1997. Effects of zero magnetic field on the conformation of chromatin in human cells. Biochimica et Biophysica Acta 1336:465-473.

Belyaev IY, Alipov YD, Matronchik AY. 1998. Cell density dependent response of E coli cells to weak ELF magnetic fields. Bioelectromagnetics 19:300-309.

Belyaev IY, Alipov YD, Matronchik AY, Radko SP. 1995. Cooperativity in E coli cell response to resonance effect of weak extremely low frequency electromagnetic field. Bioelectrochemistry and Bioenergetics 37:85-90.

Belyaev IY, Alipov YD, Polunin VA, Shcheglov VS. 1993. Evidence for dependence of resonant frequency of millimeter wave interaction with Escherichia coli Kl2 cells on haploid genome length Electro- & Magnetobiology 12:39-49.

Belyaev IY, Alipov YD, Shcheglov VS. 1992. Chromosome DNA as a target of resonant interaction between Escherichia coli cells and low-intensity millimeter waves. Electro- & Magnetobiology 11:97-108.

Belyaev IY, Alipov YD, Shcheglov VS, Lystsov VN. 1992. Resonance effect of microwaves on the genome conformational state of E coli cells. Z Naturforsch [C] 47:621-627.

Belyaev IY, Alipov YD, Shcheglov VS, Polunin VA, Aizenberg OA. 1994. Cooperative response of Escherichia coli cells to the resonance effect of millimeter waves at super low intensity. Electro- & Magnetobiology 13:53-66.

Belyaev IY, Eriksson S, Nygren J, Torudd J, Harms-Ringdahl M. 1999. Effects of ethidium bromide on DNA loop organisation in human lymphocytes measured by anomalous viscosity time dependence and single cell gel electrophoresis. Biochimica et Biophysica Acta .BBA. - General Subjects 1428:348-356.

Belyaev IY, Harms-Ringdahl M. 1996. Effects of gamma rays in the 05-50-cGy range on the conformation of chromatin in mammalian cells0 Radiation Research 145:687-693.

Belyaev IY, Hillert L, Protopopova M, Tamm C, Malmgren LOG, Persson BRR, et al. 2005. 915 MHz microwaves and 50 Hz magnetic field affect chromatin conformation and 53BP1 foci in human lymphocytes from hypersensitive and healthy persons. Bioelectromagnetics 26:173-184.

Belyaev IY, Markova E, Hillert L, Malmgren LOG, Persson BRR. 2009. Microwaves from UMTS/GSM mobile phones induce long-lasting inhibition of 53BP1/g-H2AX DNA repair foci in human lymphocytes. Bioelectromagnetics 30:129-141.

Belyaev IY, Shcheglov VS, Alipov ED, Ushakov VL. 2000. Non-thermal effects of extremely high frequency microwaves on chromatin conformation in cells in vitro:dependence on physical, physiological and genetic factors IEEE Transactions on Microwave Theory and Techniques 48.11.:2172-2179.

Belyaev IY, Shcheglov VS and Alipov YD .1992. Existence of selection rules on helicity during discrete transitions of the genome conformational state of Ecoli cells exposed to low-level millimeter radiation. Bioelectrochemistry and Bioenergetics 27:405-411.

Belyaev IY, Shcheglov VS, Alipov YD. 1992. Selection rules on helicity during discrete transitions of the genome conformational state in intact and X-rayed cells of Ecoli in millimeter range of electromagnetic field. In:Charge and Field Effects in Biosystems M Journal of Allen, S F Cleary, A E Sowers and D D Shillady Basel, Switzerland, Birkhauser 3:115-126.

Belyaev IY, Shcheglov VS, Alipov YD, Polunin VA. 1996. Resonance effect of millimeter waves in the power range from 10.-19. to 3 x 10.-3. W/cm^2 on Escherichia coli cells at different concentrations. Bioelectromagnetics 17:312-321.

Belyaev IY, Shcheglov VS, Alipov YD, Radko SP. 1993. Regularities of separate and combined effects of circularly polarized millimeter waves on E coli cells at different phases of culture growth. Bioelectrochemistry and Bioenergetics 31:49-63.

Belyaev SY, Kravchenko VG. 1994. Resonance effect of low-intensity millimeter waves on the chromatin conformational state of rat thymocytes. Zeitschrift für Naturforschung [C] Journal of biosciences 49:352-358.

Betskii OV, Devyatkov ND, Kislov VV. 2000. Low intensity millimeter waves in medicine and biology. Critical Reviews in Biomedical Engineering 28:247-268.

Binhi VN. 2002. Magnetobiology: Underlying physical problems. San Diego, Academic Press.

Binhi VN, Alipov YD, Belyaev IY. 2001. Effect of static magnetic field on E coli cells and individual rotations of ion-protein complexes. Bioelectromagnetics 22:79-86.

Blackman C. 2009. Cell phone radiation:Evidence from ELF and RF studies supporting more inclusive risk identification and assessment. Pathophysiology 16:205-216.

Blackman CF, Benane SG, Elder JA, House DE, Lampe JA, Faulk JM. 1980. Induction of calcium-ion efflux from brain tissue by radiofrequency radiation:effect of sample number and modulation frequency on the power-density window. Bioelectromagnetics 1:35-43.

Blackman CF, Benane SG, Joines WT, Hollis MA, House DE. 1980. Calcium-ion efflux from brain tissue:power-density versus internal field-intensity dependencies at 50-MHz RF radiation. Bioelectromagnetics 1:277-283.

Blank M, Goodman R. 2009. Electromagnetic fields stress living cells. Pathophysiology 16:71-78.

Bolshakov MA, Alekseev SI. 1992. Bursting responses of Lymnea neurons to microwave radiation. Bioelectromagnetics 13:119-129.

Bozhanova TP, Bryukhova AK, Golant MB. 1987. About possibility to use coherent radiation of extremely high frequency for searching differences in the state of living cells Medical and biological aspects of millimeter wave radiation of low intensity. Devyatkov ND , Fryazino IRE. Academy of Science, USSR 280 p:90-97.

Buchner K, Eger H. 2011. Changes of clinically important neurotransmitters under the influence of modulated RF fields - A long-term study under real-life conditions. Original study in German Umwelt - Medizin - Gesellschaft 24:44-57.

Burch JB, Reif JS, Noonan CW, Ichinose T, Bachand AM, KoleberTL, et al. 2002. Melatonin metabolite excretion among cellular telephone users. International Journal of Radiation Biology 78:1029-1036.

Burch JB, Reif JS, Noonan CW, Yost MG. 2000. Melatonin metabolite levels in workers exposed to 60-hz magnetic fields:Work in substations and with 3-phase conductors. Journal of Occupational and Environmental Medicine 42:136-142.

Byus CV, Kartun K, Pieper S, Adey WR. 1988. Increased ornithine decarboxylase activity in cultured cells exposed to low energy modulated microwave fields and phorbol ester tumor promoters. Cancer Research 48:4222-4226.

Byus CV, Lundak RL, Fletcher RM, Adey WR. 1984. Alterations in protein kinase activity following exposure of cultured human lymphocytes to modulated microwave fields. Bioelectromagnetics 5:341-351.

Cam ST, Seyhan N. 2012. Single-strand DNA breaks in human hair root cells exposed to mobile phone radiation. International Journal of Radiation Biology 88:420-424.

Campisi A, Gulino M, Acquaviva R, Bellia P, Raciti G, Grasso R, et al. 2010. Reactive oxygen species levels and DNA fragmentation on astrocytes in primary culture after acute exposure to low intensity microwave electromagnetic field. Neuroscience Letters 473:52-55.

Capri M, Salvioli S, Altilia S, Sevini F, Remondini D, Mesirca P, et al. 2006. Age-dependent effects of in vitro radiofrequency exposure .mobile phone. on CD95+ T helper human lymphocytes. Annals od the New York Academy of Sciences 1067:493-499.

Capri M, Scarcella E, Fumelli C, Bianchi E, Salvioli S, Mesirca P, et al. 2004. In vitro exposure of human lymphocytes to 900 MHz CW and GSM modulated radiofrequency:studies of proliferation, apoptosis and mitochondrial membrane potential. Radiation Research 16:211-218.

Caraglia M, Marra M, Mancinelli F, D'Ambrosio G, Massa R, Giordano A, et al. 2005. Electromagnetic fields at mobile phone frequency induce apoptosis and inactivation of the multi-chaperone complex in human epidermoid cancer cells. Journal of Cell Physiology 204:539-548.

Cardis E, Armstrong BK, Bowman JD, Giles GG, Hours M, Krewski D, et al. 2011. Risk of brain tumours in relation to estimated RF dose from mobile phones:results from five Interphone countries. Occupational & Environmental Medicine 68:631-640.

Chavdoula ED, Panagopoulos DJ, Margaritis LH. 2010. Comparison of biological effects between continuous and intermittent exposure to GSM-900-MHz mobile phone radiation:Detection of apoptotic cell-death features. Mutation Research 700:51-61.

Chiabrera A, Bianco B, Caufman JJ, Pilla AA. 1991. Quantum dynamics of ions in molecular crevices under electromagnetic exposure. In:Electromagnetics in Medicine and Biology, Brighton ct & Pollack SR. San Francisco, San Francisco Press:21-26.

Chiabrera A, Bianco B, Moggia E, Kaufman JJ. 2000. Zeeman-Stark modeling of the RF EMF interaction with ligand binding. Bioelectromagnetics 21:312-324.

Cifra M, Fields JZ, Farhadi A. 2011. Electromagnetic cellular interactions. Progress in Biophysics and Molecular Biology 105:223-246.

Cook CM, Saucier DM, Thomas AW, Prato FS. 2006. Exposure to ELF magnetic and ELF-modulated radiofrequency fields:the time course of physiological and cognitive effects observed in recent studies. 2001-2005. Bioelectromagnetics 27:613-627.

Croft RJ, Chandler JS, Burgess AP, Barry RJ, Williams JD, Clarke AR. 2002. Acute mobile phone operation affects neural function in humans. Clinical Neurophysiology 113:1623-1632.

Czerska EM, Elson EC, Davis CC, Swicord ML, Czerski P. 1992. Effects of continuous and pulsed 2450-MHz radiation on spontaneous lymphoblastoid transformation of human lymphocytes in vitro. Bioelectromagnetics 13:247-259.

Czyz J, Guan K, Zeng Q, Nikolova T, Meister A, Schönborn F, et al. 2004. High frequency electromagnetic fields .GSM signals. affect gene expression levels in tumor suppressor p53-deficient embryonic stem cells Bioelectromagnetics 25:296-307.

d'Ambrosio G, Massa R, Scarfi MR, Zeni O.Schuderer J, Kuster N, Wobus AM. 2002. Cytogenetic damage in human lymphocytes following GMSK phase modulated microwave exposure. Bioelectromagnetics 23:7-13.

Davanipour Z, Sobel E .2009. Long-term exposure to magnetic fields and the risks of Alzheimer's disease and breast cancer: Further biological research. Pathophysiology 16:149-156.

De Iuliis GN, Newey RJ, King BV, Aitken RJ. 2009. Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro. PLoS One 4:e6446.

Del Vecchio G, Giuliani A, Fernandez M, Mesirca P, Bersani F, Pinto R, et al. 2009. Effect of radiofrequency electromagnetic field exposure on in vitro models of neurodegenerative disease. Bioelectromagnetics 30:564-572.

Devyatkov N.D. 1973. Influence of electromagnetic radiation of millimeter range on biological objects. In Russian. Usp Fiz Nauk 116:453-454.

Devyatkov ND, Golant MB, Betskij OV.1994. Peculiarities of usage of millimeter waves in biology and medicine. In Russian. Moscow, IRE RAN.

Di Carlo A, White N, Guo F, Garrett P, Litovitz T. 2002. Chronic electromagnetic field exposure decreases HSP70 levels and lowers cytoprotection. Journal of Cell Biochem 84:447-454.

Diem E, Schwarz C, Adlkofer F, Jahn O, Rüdiger H. 2005. Non-thermal DNA breakage by mobile-phone radiation .1800 MHz. in human fibroblasts and in transformed GFSH-R17 rat granulosa cells in vitro. Mutation Research 583:178-183.

Dolgacheva LP, Semenova TP, Abzhalelov BB, Akoev IG. 2000. [The effect of electromagnetic radiation on the monoamine oxidase A activity in the rat brain.] Radiatsionnaia Biologiia, Radioecologiia 40:429-432.

Dragicevic N, Bradshaw PC, Mamcarz M, Lin X, Wang L, Cao C, et al. 2011. Long-term electromagnetic field treatment enhances brain mitochondrial function of both Alzheimer's transgenic mice and normal mice:a mechanism for electromagnetic field-induced cognitive benefit? Neuroscience 185:135-49..

Duan Y, Zhang HZ, Bu RF. 2011. Correlation between cellular phone use and epithelial parotid gland malignancies. International Journal of Oral Maxillofacial Surgery 40:966-972.

Dutta SK, Ghosh B, Blackman CF. 1989. Radiofrequency radiation-induced calcium ion efflux enhancement from human and other neuroblastoma cells in culture. Bioelectromagnetics 10:197-202.

Dutta SK, Subramoniam A, Ghosh B, Parshad R. 1984. Microwave radiation-induced calcium ion efflux from human neuroblastoma cells in culture. Bioelectromagnetics 5:71-78.

Eberhardt JL, Persson BR, Brun AE, Salford LG, Malmgren LO. 2008. Blood-brain barrier permeability and nerve cell damage in rat brain 14 and 28 days after exposure to microwaves from GSM mobile phones. Electromagnetic Biology & Medicine 27:215-229.

Elhag MA, Nabil GM, Attia AM. 2007. Effects of electromagnetic field produced by mobile phones on the oxidant and antioxidant status of rats. Pakistan Journal of Biological Sciences 10:4271-4274.

Esmekaya MA, Aytekin E, Ozgur E, Güler G, Ergun MA, Omeroğlu S, et al. 2011. Mutagenic and morphologic impacts of 18GHz radiofrequency radiation on human peripheral blood lymphocytes .hPBLs. and possible protective role of pre-treatment with Ginkgo biloba (EGb 761). Science of the Total Environment 410-411:59-64.

Fisher PD, Poznansky MJ, Voss VA. 1982. Effect of microwave radiation .2450 MHz. on the active and passive components of 24Na+ efflux from human erythrocytes. Radiation Research 92:411-422.

Foster KR, Repacholi MH. 2004. Biological effects of radiofrequency fields:does modulation matter? Radiation Research 162:219-225.

Franzellitti S, Valbonesi P, Ciancaglini N, Biondi C, Contin A, Bersani F, et aL. 2010. Transient DNA damage induced by high-frequency electromagnetic fields .GSM 18 GHz. in the human trophoblast HTR-8/SVneo cell line evaluated with the alkaline comet assay. Mutation Research 683:35-42.

Franzellitti S, Valbonesi P, Biondi C, Contin A, Fabbri E. 2008. HSP70 expression in human trophoblast cells exposed to different 18 Ghz mobile phone signals. Radiation Research 170:488-497.

Frei P, Mohler E, Bürgi A, Fröhlich J, Neubauer G, Braun-Fahrländer C, et al. 2010. Classification of personal exposure to radio frequency electromagnetic fields .RF-EMF. for epidemiological research: Evaluation of different exposure assessment methods. Environment International 36:714-720.

Frei P, Mohler E, Neubauer G, Theis G, Bürgi A, Fröhlich J, et al. 2009. Temporal and spatial variability of personal exposure to radio frequency electromagnetic fields. Environmental Research 109:779-785.

French PW, Donnellan M, McKenzie DR. 1997. Electromagnetic radiation at 835 MHz changes the morphology and inhibits proliferation of a human astrocytoma cell line. Bioelectrochemistry & Bioenergetics 43:13-18.

Frey AH. 1967. Brain stem evoked responses associated with low-intensity pulsed UHF energy. Journal of Applied Physiology 23:984-988.

Frey AH. 1974. Differential biologic effects of pulsed and continuous electromagnetic fields and mechanisms of effect. Annals of the New York Academy of Sciences 238:273-279.

Frey AH. 1993. Electromagnetic field interactions with biological systems. FASEB Journal 7:272-281.

Friedman J, Kraus S, Hauptman Y, Schiff Y, Seger R. 2007. Mechanism of short-term ERK activation by electromagnetic fields at mobile phone frequencies. The Biochemical Journal 405:559-568.

Frohlich H. 1968. Long-range coherence and energy storage in biological systems. International Journal of Quantum Chemistry 2:641-652.

Gajski G, Garaj-Vrhovac V. 2009. Radioprotective effects of honeybee venom .Apis mellifera. against 915-MHz microwave radiation-induced DNA damage in Wistar rat lymphocytes: in vitro study. International Journal of Toxicology 28:88-98.

Gapeev AB, IakushinaVS, Chemeris NK, Fesenko EE. 1997. Modulated extremely high frequency electromagnetic radiation of low intensity activates or inhibits respiratory burst in neutrophils depending on modulation frequency. In Russian. Biofizika 425:1125-1134.

Gapeev AB, IakushinaVS, Chemeris NK, Fesenko EE. 1999. Dependence of EHF EMF effects on the value of the static magnetic field. Dokl Akad Nauk 369.404-407.

Gapeev AB, IakushinaVS, Chemeris NK, Fesenko EE. 1996. [Modification of the activity of murine peritoneal neutrophils upon exposure to millimeter waves at close and far distances from the emitter.] Biofizika 41:205-219.

Gapeev AB, Mikhailik EN, Chemeris NK. 2008. Anti-inflammatory effects of low-intensity extremely high-frequency electromagnetic radiation: Frequency and power dependence. Bioelectromagnetics 29:197-206.

Gapeev AB, Mikhailik EN, Chemeris NK. 2009. Features of anti-inflammatory effects of modulated extremely high-frequency electromagnetic radiation. Bioelectromagnetics 30:454-61.

Gapeev AB, SafronovaVG, Chemeris NK, Fesenko EE. 1997. Inhibition of the production of reactive oxygen species in mouse peritoneal neutrophils by millimeter wave radiation in the near and far field zones of the radiator. Bioelectrochemistry & Bioenergetics 43:217-220.

Gapeev AB, Yakushina VS, Chemeris NK, Fesenko EE. 1998. Modification of production of reactive oxygen species in mouse peritoneal neutrophils on exposure to low-intensity modulated millimeter wave radiation. Bioelectrochemistry & Bioenergetics 46:267-272.

Gerner C, Haudek V, Schandl U, Bayer E, Gundacker N, Hutter HP, et al. 2010. Increased protein synthesis by cells exposed to a 1,800-MHz radio-frequency mobile phone electromagnetic field, detected by proteome profiling. International Archives of Occupational and Environmental Health 83:691-702.

Golant MB. 1989. Resonance effect of coherent millimeter-band electromagnetic waves on living organisms. In Russian. Biofizika 34:1004-1014.

Golant MB, Kuznetsov AP, Bozhanova TP. 1994. The mechanism of synchronizing yeast cell cultuResearch with EHF-radiation. In Russian. Biofizika 39:490-495.

Golo VL. 2005. Three-wave interaction between interstrand modes of the DNA. Journal of Experimental and Theoretical Physics 101:372-379.

Gos P, Eicher B. Kohli J, Heyer WD. 1997. Extremely high frequency electromagnetic fields at low power density do not affect the division of exponential phase Saccharomyces cerevisiae cells. Bioelectromagnetics 18:142-155.

Grigoriev Y, Nikitina V, Rubtcova N, Pokhodzey L, Grigoriev O, Belyaev I, et al. 2005. The Russian National Committee on Non-Ionizing Radiation Protection .RNCNIRP. and the radiation guidelines Transparency Forum for Mobile Telephone Systems, Stockholm, Available at:http://memberschellose/igorbelyaev/guidelinespdf

Grigoriev YG. 2004. Bioeffects of modulated electromagnetic fields in the acute experiments .results of Russian researches. Annual of Russian National Committee on Non-Ionisng Radiation Protection Moscow, ALLANA:16-73

Grigoriev YG, StepanovVS, Nikitina VN, Rubtcova NB, Shafirkin AV, Vasin VL. 2003. ISTC Report Biological effects of radiofrequency electromagnetic fields and the radiation guidelines. Results of experiments performed in Russia/Soviet Union Moscow, Institute of Biophysics, Ministry of Health, Russian Federation.

Grundler W. 1992. Intensity- and frequency-dependent effects of microwaves on cell growth rates. Bioelectrochemistry & Bioenergetics 27:361-365.

Grundler W, Jentzsch V, Keilmann F, Putterlik V. 1988. Resonant cellular effects of low intensity microwaves. Biological Coherence and Response to External Stimuli H Frцlich Berlin, Springer-Verlag:65-85.

Guler G, Tomruk A, Ozgur E, Sahin D, Sepici A, Altan N, et al. 2012. The effect of radiofrequency radiation on DNA and lipid damage in female and male infant rabbits. International Journal of Radiation Biology 88:367-373.

Guney M, Ozguner F, Oral B, Karahan N, Mungan T. 2007. 900 MHz radiofrequency-induced histopathologic changes and oxidative stress in rat endometrium:protection by vitamins E and C. Toxicology & Industrial Health 23:411-420.

Hardell L, Carlberg M. 2009. Mobile phones, cordless phones and the risk for brain tumours. International Journal of Oncology 35:5-17.

Hardell L , Carlberg M, Hansson Mild K. 2009. Epidemiological evidence for an association between use of wireless phones and tumor diseases. Pathophysiology 16:113-22.

Hardell L, Eriksson M, Carlberg M, Sundström C, Mild KH. 2005. Use of cellular or cordless telephones and the risk for non-Hodgkin's lymphoma. International Archives of Occupational and Environmental Health DOI 101007/s00420-005-0003-5

Hardell L, Mild KH. 2005. Mobile phone use and acoustic neuromas Epidemiology 16:415; author reply 417-418.

Hardell L, Mild KH, Carlberg M. 2003. Further aspects on cellular and cordless telephones and brain tumours. International Journal of Oncology 22:399-407.

Hardell L, Mild KH, Pahlson A, Hallquist A. 2001. Ionizing radiation, cellular telephones and the risk for brain tumours. European Journal of Cancer Prevention 10:523-529.

Hardell L, Mild KH, Carlberg M, Hallquist A. 2004. Cellular and cordless telephone use and the association with brain tumors in different age groups. Archives of Environmental Health 59:132-137.

Heath B, Jenvey S, Cosic I. 1998. Investigation of analogue and digital mobile phone low frequency radiation spectrum characteristics. Proceedings of the 2nd International Conference on Bioelectromagnetism 83-84.

Hinrikus H, Bachmann M, Lass J, Tomson R, Tuulik V. 2008. Effect of 7, 14 and 21 Hz modulated 450 MHz microwave radiation on human electroencephalographic rhythms. International Journal of Radiation Biology 84:69-79.

Hintzsche H, Jastrow C, Kleine-Ostmann T, Stopper H, Schmid E, Schrader T. 2011. Terahertz radiation induces spindle disturbances in human-hamster hybrid cells. Radiation Research 175:569-574.

Hoyto A, Naarala JJ, 2007. Ornithine decarboxylase activity is affected in primary astrocytes but not in secondary cell lines exposed to 872 MHz RF radiation. International Journal of Radiation Biology 83:367-374.

Höytö A, Luukkonen J, Juutilainen J, Naarala J. 2008. Proliferation, oxidative stress and cell death in cells exposed to 872 MHz radiofrequency radiation and oxidants. Radiation Research 170:235-243.

Huber R, Treyer V, Borbély AA, Schuderer J, Gottselig JM, Landolt HP, et al. 2002. Electromagnetic fields, such as those from mobile phones, alter regional cerebral blood flow and sleep and waking. EEG Journal of Sleep Research 11:289-295.

Huber, R, Treyer V, Schuderer J, Berthold T, Buck A, Kuster N, et al. 2005. Exposure to pulse-modulated radio frequency electromagnetic fields affects regional cerebral blood flow. European Journal of Neuroscience 21:1000-1006.

Huss A, Egger M, Hug K, Huwiler-Müntener K, Röösli M. 2007. Source of funding and results of studies of health effects of mobile phone use:systematic review of experimental studies. Environmental Health Perspectives 115:1-4.

Huttunen P, Hanninen O , Myllyla R. 2009. FM-radio and TV tower signals can cause spontaneous hand movements near moving RF reflector. Pathophysiology 16:201-204.

Hyland GJ. 2000. Physics and biology of mobile telephony. Lancet 356(9244):1833-1836.

IARC. 2002. Biennial Report 2002-2003. Lyon, France, IARC Press 80:183.

ICNIRP. 1998. ICNIRP Guidelines Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields .up to 300 GHz. Health Physics 74:494-522.

Ilhan A, Gurel A, Armutcu F, Kamisli S, Iraz M, Akyol O, et al. 2004. Ginkgo biloba prevents mobile phone-induced oxidative stress in rat brain. Clinical Chim Acta 340:153-162.

Ilvonen S, Sihvonen AP, Karkkainen K, Sarvas K. 2005. Numerical assessment of induced ELF currents in the human head due to the battery current of a digital mobile phone. Bioelectromagnetics 26:648-656.

Imge EB, Kilicoglu B, Devrim E, Cetin R, Durak I. 2010. Effects of mobile phone use on brain tissue from the rat and a possible protective role of vitamin C - a preliminary study. International Journal of Radiation Biology 86:1044-1049.

Iskin VD. 1990. Biological effects of millimeter waves and correlation method of their detection. In Russian. Kharkov, Osnova.

Johansson PA, Cappello S, Gotz M. 2010. Stem cells niches during development--lessons from the cerebral cortex. Current Opinions in Neurobiology 20:400-407.

Joines WT, Blackman CF. 1980. Power density, field intensity, and carrier frequency determinants of RF-energy-induced calcium-ion efflux from brain tissue. Bioelectromagnetics 1:271-275.

Jokela K, Puranen L, Sihvonen AP. 2004. Assessment of the magnetic field exposure due to the battery current of digital mobile phones. Health Physics 86:56-66.

Jorge-Mora T, Misa-Agustiño MJ, Rodríguez-González JA, Jorge-Barreiro FJ, Ares-Pena FJ, López-Martín E. 2011. The effects of single and repeated exposure to 245 GHz radiofrequency fields on c-fos protein expression in the paraventricular nucleus of rat hypothalamus. Neurochemical Research 36:2322-2332.

Joseph W, Frei P, Roösli M, Thuróczy G, Gajsek P, Trcek T, et al. 2010. Comparison of personal radio frequency electromagnetic field exposure in different urban areas across Europe. Environmental Research 110:658-663.

Juutilainen J, Hoyto A, Kumlin T, Naarala J. 2011. Review of possible modulation-dependent biological effects of radiofrequency fields. Bioelectromagnetics 32:511-34.

Kabuto M, Nitta H, Yamamoto S, Yamaguchi N, Akiba S, Honda Y, et al. 2006. Childhood leukemia and magnetic fields in Japan:a case-control study of childhood leukemia and residential power-frequency magnetic fields in Japan. International Journal of Cancer 119:643-650.

Kazanis I. 2012. Can adult neural stem cells create new brains? Plasticity in the adult mammalian neurogenic niches:realities and expectations in the era of regenerative biology. Neuroscientist 18:15-27.

Kim TH, Shivdasani RA. 2012. Stem cell niches: famished paneth cells, gluttonous stem cells. Current Biology 22:R579-580.

Kolbun ND, Lobarev VE. 1988. Problems of bioinformational interaction in millimeter range. In Russian. Kibernet Vychislitelnaya Tekhnika 78:94-99.

Koveshnikova IV, Antipenko EN. 1991. [On the quantitative regularities of the cytogenic effect of microwaves] Radiobiologiia 31:149-151.

Köylü H, Mollaoglu H, Ozguner F, Naziroglu M, Delibas N. 2006. Melatonin modulates 900 Mhz microwave-induced lipid peroxidation changes in rat brain. Journal of Toxicology and Industrial Health 22:211-216.

Kundi M, Mild K, Hardell L, Mattsson MO. 2004. Mobile telephones and cancer - a review of epidemiological evidence. Journal of Toxicology & Environmental Health B. Critical Reviews 7:351-384.

Kwee S, Raskmark P. 1998. Changes in cell proliferation due to environmental non-ionizing radiation 2 Microwave radiation. Bioelectrochemistry & Bioenergetics 44:251-255.

Lagroye I, Anane R, Wettring BA, Moros EG, Straube WL, Laregina M, et al. 2004. Measurement of DNA damage after acute exposure to pulsed-wave 2450 MHz microwaves in rat brain cells by two alkaline comet assay methods. International Journal of Radiation Biology 80:11-20.

Lai H. 2004. Interaction of microwaves and a temporally incoherent magnetic field on spatial learning in the rat. Physiology Behavior 82:785-789.

Lai H. 2005. Biological effects of radiofrequency electromagnetic field. Encyclopedia of Biomaterials and Biomedical Engineering. Wnek GE & Bowlin GI, New York, NY, Marcel Decker:1-8.

Lai H, Singh NP. 1995. Acute low-intensity microwave exposure increases DNA single-strand breaks in rat brain cells. Bioelectromagnetics 16:207-210.

Lai H, Singh NP. 1996. Single- and double-strand DNA breaks in rat brain cells after acute exposure to radiofrequency electromagnetic radiation. International Journal of Radiation Biology 69:513-521.

Lai H, Singh NP. 1997. Melatonin and a spin-trap compound block radiofrequency electromagnetic radiation-induced DNA strand breaks in rat brain cells. Bioelectromagnetics 18:446-454.

Lai H, Singh NP. 2005. Interaction of microwaves and a temporally incoherent magnetic field on single and double DNA strand breaks in rat brain cells. Electromagnetic Biology & Medicine 24:23-29.

Liburdy RP, Vanek, PF Jr. 1985. Microwaves and the cell membrane II Temperature, plasma, and oxygen mediate microwave-induced membrane permeability in the erythrocyte. Radiation Research 102:190-205.

Liburdy RP, Vanek, PF Jr. 1987. Microwaves and the cell membrane III Protein shedding is oxygen and temperature dependent:evidence for cation bridge involvement. Radiation Research 109:382-395.

Lin-Liu S, Adey WR. 1982. Low frequency amplitude modulated microwave fields change calcium efflux rates from synaptosomes. Bioelectromagnetics 3:309-322.

Linde T, Mild KH. 1997. Measurement of low frequency magnetic fields from digital cellular telephones. Bioelectromagnetics 18:184-186.

Litovitz TA, Krause D, Penafiel M, Elson EC, Mullins JM. 1993. The role of coherence time in the effect of microwaves on ornithine decarboxylase activity. Bioelectromagnetics 14:395-403.

Litovitz TA, Penafiel M, Farrel JM, Krause D, Meister R, and Mullins JM. 1997. Bioeffects induced by exposure to microwaves are mitigated by superposition of ELF noise. Bioelectromagnetics 18:422-430.

Lonn S, Ahlbom A, Hall P, Feychting M. 2004. Mobile phone use and the risk of acoustic neuroma. Epidemiology 15:653-659.

López-Martín E, Bregains J, Relova-Quinteiro JL, Cadarso-Suárez C, Jorge-Barreiro FJ, Ares-Pena FJ. 2009. The action of pulse-modulated GSM radiation increases regional changes in brain activity and c-Fos expression in cortical and subcortical areas in a rat model of picrotoxin-induced seizure proneness. Journal of Neuroscience Research 87:1484-1499.

Lu YS, Huang BT, Huang YX. 2012. Reactive oxygen species formation and apoptosis in human peripheral blood mononuclear cell induced by 900 MHz mobile phone radiation. Oxidative Medicine & Cellular Longevity 2012:740280.

Lukashevsky KV, Belyaev IY. 1990. Switching of prophage lambda genes in Escherichia coli by millimeter waves. Medical Science Research I8:955-957.

Malyapa RS, Ahern EW, Bi C, Straube WL, LaRegina M, Pickard WF, et al. 1998. DNA damage in rat brain cells after in vivo exposure to 2450 MHz electromagnetic radiation and various methods of euthanasia. Radiation Research 149:637-645.

Malyapa RS, Ahern EW, Straube WL, Moros EG, Pickard WF, Roti Roti JL. 1997. Measurement of DNA damage after exposure to 2450 MHz electromagnetic radiation. Radiation Research 148:608-617.

Markkanen A, Penttinen P, Naarala J, Pelkonen J, Sihvonen AP, Juutilainen J. 2004. Apoptosis induced by ultraviolet radiation is enhanced by amplitude modulated radiofrequency radiation in mutant yeast cells. Bioelectromagnetics 25:127-133.

Markovà E, Hillert L, Malmgren L, Persson BR, Belyaev IY. 2005. Microwaves from GSM mobile telephones affect 53BP1 and gamma-H2AX foci in human lymphocytes from hypersensitive and healthy persons. Environmental Health Perspectives 113:1172-1177.

Markovà E, Malmgren LOG, Belyaev IY. 2010. Microwaves from mobile phones inhibit 53BP1 focus formation in human stem cells more strongly than in differentiated cells:possible mechanistic link to cancer risk. Environmental Health Perspectives 118:394-399.

Matronchik AI, Alipov ED, Beliaev IY. 1996. A model of phase modulation of high frequency nucleoid oscillations in reactions of E coli cells to weak static and low-frequency magnetic fields. In Russian. Biofizika 41:642-649.

Matronchik AI, Beliaev IY. 2005. Model of slow nonuniform rotation of the charged DNA domain for effects of microwaves, static and alternating magnetic fields on conformation of nucleoid in living cells. Fröhlich Centenary International Symposium Coherence and Electromagnetic Fields in Biological Systems .CEFBIOS-2005. Journal of Pokorny Prague, Czech Republic, Institute of Radio Engineering and Electronics, Academy of Sciences of the Czech Republic:63-64.

Matronchik AI, Beliaev IY. 2008. Mechanism for combined action of microwaves and static magnetic field: slow non uniform rotation of charged nucleoid. Electromagnetic Biology & Medicine 27:340-354.

Metcalfe AD, Ferguson MW. 2008. Skin stem and progenitor cells:using regeneration as a tissue-engineering strategy. Cellular & Molecular Life Sciences 65:24-32.

Morrison SJ, Spradling AC. 2008. Stem cells and niches: mechanisms that promote stem cell maintenance throughout life. Cell 132:598-611.

Nam KC, Kim SW, Kim SC, Kim DW. 2006. Effects of RF exposure of teenagers and adults by CDMA cellular phones. Bioelectromagnetics 27:509-514.

Nazıroğlu M, Ciğ B, Doğan S, Uğuz AC, Dilek S, Faouzi D. 2012. 245-Gz wireless devices induce oxidative stress and proliferation through cytosolic Ca^{2+} influx in human leukemia cancer cells. International Journal of Radiation Biology 88:449-456.

Nikolova T, Czyz J, Rolletschek A, Blyszczuk P, Fuchs J, Jovtchev G, et al. 2005. Electromagnetic fields affect transcript levels of apoptosis-related genes in embryonic stem cell-derived neural progenitor cells. FASEB Journal 19:1686-1688.

Niwa O. 2010. Roles of stem cells in tissue turnover and radiation carcinogenesis. Radiation Research 174:833-839.

Nylund R, Leszczynski D. 2006. Mobile phone radiation causes changes in gene and protein expression in human endothelial cell lines and the response seems to be genome- and proteome-dependent. Proteomics 6:4769-4780.

Oktem F, Ozguner F, Mollaoglu H, Koyu A, Uz E. 2005. Oxidative damage in the kidney induced by 900-MHz-emitted mobile phone:protection by melatonin. Archives of Medical Research 36:350-355.

Olcerst RB, Belman S, Eisenbud M, Mumford WW, Rabinowitz JR. 1980. The increased passive efflux of sodium and rubidium from rabbit erythrocytes by microwave radiation. Radiation Research 82:244-256.

Oscar KJ, Hawkins TD. 1977. Microwave alteration of the blood-brain barrier system of rats. Brain Research 126:281-293.

Ozguner F, Altinbas A, Ozaydin M, Dogan A, Vural H, Kisioglu AN, et al. 2005. Mobile phone-induced myocardial oxidative stress:protection by a novel antioxidant agent caffeic acid phenethyl ester. Toxicology & Industrial Health 21:223-230.

Ozguner F, Aydin G, Mollaoglu H, Gökalp O, Koyu A, Cesur G. 2004. Prevention of mobile phone induced skin tissue changes by melatonin in rat: an experimental study. Toxicology & Industrial Health 20:133-139.

Ozguner F, Bardak Y, Comlekci C. 2006. Protective effects of melatonin and caffeic acid phenethyl ester against retinal oxidative stress in long-term use of mobile phone: a comparative study. Molecular & Cellular Biochemistry 282:83-88.

Ozguner F, Oktem F, Armagan A, Yilmaz R, Koyu A, Demirel R, et al. 2005. Comparative analysis of the protective effects of melatonin and caffeic acid phenethyl ester .CAPE. on mobile phone-induced renal impairment in rat. Molecular & Cellular Biochemistry 276:31-37.

Ozguner F, Oktem F, Ayata A, Koyu A, Yilmaz HR. 2005. A novel antioxidant agent caffeic acid phenethyl ester prevents long-term mobile phone exposure-induced renal impairment in rat. Prognostic value of malondialdehyde, N-acetyl-beta-D-glucosaminidase and nitric oxide determination. Molecular & Cellular Biochemistry 277:73-80.

Ozgur E, Gler G, Seyhan N. 2010. Mobile phone radiation-induced free radical damage in the liver is inhibited by the antioxidants n-acetyl cysteine and epigallocatechin-gallate. International Journal of Radiation Biology 86:935-945.

Pakhomov AG, Akyel Y, Pakhomova ON, Stuck BE, Murphy MR. 1998. Current state and implications of research on biological effects of millimeter waves: a review of the literature. Bioelectromagnetics 19:393-413.

Pakhomov AG, and Murphy MR. 2000. Comprehensive review of the research on biological effects of pulsed radiofrequency radiation in Russia and the former Soviet Union. Advances in Electromagnetic Fields in Living System JC Lin New York, Kluwer Academic/Plenum Publishers 3:265-290.

Pakhomov AG, Murthy PR. 2000. Low-intensity millimeter waves as a novel therapeutic modality. IEEE Transactions on Plasma Science 28:34-40.

Panagopoulos DJ, Karabarbounis A, Margaritis LH. 2002. Mechanism for action of electromagnetic fields on cells. Biochemical & Biophysical Research Communications 298:95-102.

Panagopoulos DJ, Margaritis LH. 2010. The effect of exposure duration on the biological activity of mobile telephony radiation. Mutation Research 699:17-22.

Papageorgiou CC, Nanou ED, Tsiafakis VG, Capsalis CN, Rabavilas AD. 2004. Gender related differences on the EEG during a simulated mobile phone signal. Neuroreport 15:2557-2560.

Pashovkina MS, Akoev IG. 2000a. [Changes in serum alkaline phosphatase activity during in vitro exposure to amplitude-modulated electromagnetic field of ultrahigh frequency .2375 MHz. in guinea pigs] Biofizika 45:130-136.

Pashovkina MS, Akoev IG. 2001b. [Effect of low-intensity pulse-modulated microwave on human blood aspartate aminotransferase activity] Radiatsionnaia biologiia, radioecologiia 41:59-61.

Pashovkina MS, Akoev IG. 2001c. [Effect of low intensity pulse-modulated electromagnetic radiation on activity of alkaline phosphatase in blood serum] Radiatsionnaia Biologiia, Radioecologiia 41:62-66.

Peinnequin A, Piriou A, Mathieu J, Dabouis V, Sebbah C, Malabiau R, et al. 2000. Non-thermal effects of continuous 245 GHz microwaves on Fas-induced apoptosis in human Jurkat T-cell line. Bioelectrochemistry 51:157-161.

Penafiel LM, Litovitz T, Krause D, Desta A, Mullins JM. 1997. Role of modulation on the effect of microwaves on ornithine decarboxylase activity in L929 cells. Bioelectromagnetics 182:132-141.

Perentos N, Iskra S, McKenzie RJ, Cosi I. 2007. Characterization of pulsed ELF magnetic fields generated by GSM mobile phone handsets. World Congress on Medical Physics and Biomedical Engineering 2006, Vol 14, Pts 1-6 14:2706-2709.

Perentos N, Iskra S, McKenzie RJ, Cosi I. 2008. Simulation of pulsed ELF magnetic fields generated by GSM mobile phone handsets for human electromagnetic bioeffects research. Australasian Physical & Engineering Sciences in Medicine 31:235-242.

Persson BRR, Salford KG, Brun A. 1997. Blood-Brain Barrier permeability in rats exposed to electromagnetic fields used in wireless communication. Wireless Networks 3:455-461.

Phillips JL, Singh NP, Lai H. 2009. Electromagnetic fields and DNA damage. Pathophysiology 16:79-88.

Pollycove M, Feinendegen LE. 2003. Radiation-induced versus endogenous DNA damage: possible effect of inducible protective responses in mitigating endogenous damage. Human & Experimental Toxicology 22:290-306.

Postow E, Swicord ML. 1986. Modulated fields and window effects. CRC Handbook of Biological Effects of Electromagnetic Fields C Polk and E Postow Boca Raton, FL, CRC Press:425-460.

Presman AS. 1963. [Problems in the Biological Action of Microwaves] Usp Sovrem Biol 56:161-179.

Presman AS, IuI L, Levitina MA. 1961. [Biological effect of microwaves] Usp Sovrem Biol 51:84-103.

Remondini D, Nylund R, Reivinen J, Poulletier de Gannes F, Veyret B, et al. 2006. Gene expression changes in human cells after exposure to mobile phone microwaves. Proteomics 6:4745-4754.

Repacholi MH, Basten A, Gebski V, Noonan D, Finnie J, Harris AW. 1997. Lymphomas in E mu-Pim1 transgenic mice exposed to pulsed 900 MHZ electromagnetic fields. Radiation Research 1475:631-640.

Richardson RB. 2011. Stem cell niches and other factors that influence the sensitivity of bone marrow to radiation-induced bone cancer and leukaemia in children and adults. International Journal of Radiation Biology 87:343-359.

Salford LG, Brun A, Sturesson K, Eberhardt JL, Persson BR. 1994. Permeability of the blood-brain barrier induced by 915 MHz electromagnetic radiation, continuous wave and modulated at 8, 16, 50, and 200 Hz. Microscopy Research & Technique. 27:535-542.

Sannino A, Sarti M, Reddy SB, Prihoda TJ, Vijayalaxmi, Scarfì MR. 2009. Induction of adaptive response in human blood lymphocytes exposed to radiofrequency radiation. Radiation Research 171:735-742.

Santini R, Seigne M, Bonhomme-Faivre L, Bouffet S, Defrasne E, Sage M. 2001. [Symptoms reported by mobile cellular telephone users] Pathologie-biologie. Paris. 49:222-226.

Sarimov R, Alipov ED, Belyaev IY. 2011. Fifty hertz magnetic fields individually affect chromatin conformation in human lymphocytes:dependence on amplitude, temperature, and initial chromatin state. Bioelectromagnetics 32:570-579.

Sarimov R, Malmgren L, Markova E, Persson B, Belyaev IY. 2004. Non-thermal GSM microwaves affect chromatin conformation in human lymphocytes similar to heat shock. IEEE Transactions on Plasma Science 32:1600-1608.

Schrader T, Münter K, Kleine-Ostmann T, Schmid E. 2008. Spindle disturbances in human-hamster hybrid .AL. cells induced by mobile communication frequency range signals. Bioelectromagnetics 29:626-639.

Schwarz C, Kratochvil E, Pilger A, Kuster N, Adlkofer F, Rüdiger HW. 2008. Radiofrequency electromagnetic fields .UMTS, 1,950 MHz. induce genotoxic effects in vitro in human fibroblasts but not in lymphocytes. International Archives of Occupational Environmental Health 81:755-767.

Sevast'yanova, L A .1981. Nonthermal effects of millimeter radiation. In Russian. Devyatkov ND. Moscow, Institute of Radioelctronics of USSR Academy of Science:86-109.

Shcheglov VS, Alipov ED, Belyaev IY. 2002. Cell-to-cell communication in response of E coli cells at different phases of growth to low-intensity microwaves. Biochimica et Biophysica Acta 1572:101-106.

Shcheglov VS, Belyaev IY, Ushakov VL, Alipov YD. 1997. Power-dependent rearrangement in the spectrum of resonance effect of millimeter waves on the genome conformational state of E coli cells. Electro- & Magnetobiology 16:69-82.

Shckorbatov YG, Grigoryeva NN, Shakhbazov VG, Grabina VA, Bogoslavsky AM. 1998. Microwave irradiation influences on the state of human cell nuclei. Bioelectromagnetics 19:414-419.

Shckorbatov YG, Pasiuga VN, Goncharuk EI, Petrenko TP, Grabina VA, Kolchigin NN, et al. 2010. Effects of differently polarized microwave radiation on the microscopic structure of the nuclei in human fibroblasts. Journal of Zhejiang University Science B 11:801-805.

Shckorbatov YG, Pasiuga VN, Kolchigin NN, Grabina VA, Batrakov DO, Kalashnikov VV, et al. 2009. The influence of differently polarised microwave radiation on chromatin in human cells. International Journal of Radiation Biology 85:322-329.

Sit'ko SP, Ed .1989. The 1st All-Union Symposium with International Participation Use of Millimeter Electromagnetic Radiation in Medicine. Kiev, Ukraine, USSR, TRC Otklik.

Smythe JW, Costall B. 2003. Mobile phone use facilitates memory in male, but not female, subjects. Neuroreport 14:243-246.

Sokolovic D, Djindjic B, Nikolic J, Bjelakovic G, Pavlovic D, Kocic G, et al. 2008. Melatonin reduces oxidative stress induced by chronic exposure of microwave radiation from mobile phones in rat brain. Journal of Radiation Research 49:579-586.

Stagg RB, Thomas WJ, Jones RA, Adey WR. 1997. DNA synthesis and cell proliferation in C6 glioma and primary glial cells exposed to a 83655 MHz modulated radiofrequency field. Bioelectromagnetics 18:230-236.

Sugiyama T, Nagasawa T. 2012. Bone marrow niches for hematopoietic stem cells and immune cells. Inflammation & Allergy Drug Targets 11:201-206.

Sun W, Shen X, Lu D, Fu Y, Lu D, Chiang H. 2012. A 18-GHz radiofrequency radiation induces EGF receptor clustering and phosphorylation in cultured human amniotic (FL) cells. International Journal of Radiation Biology 88:239-244.

Tkalec M, Malarić K, Pavlica M, Pevalek-Kozlina B, Vidaković-Cifrek Z. 2009. Effects of radiofrequency electromagnetic fields on seed germination and root meristematic cells of Allium cepa L. Mutation Research - Genetic Toxicology & Environmental Mutagenesis 672:76-81.

Tkalec M, Malarić K, Pevalek-Kozlina B. 2005. Influence of 400, 900, and 1900 MHz electromagnetic fields on Lemna minor growth and peroxidase activity. Bioelectromagnetics 26:185-193.

Tkalec M, Malarić K, Pevalek-Kozlina B. 2007. Exposure to radiofrequency radiation induces oxidative stress in duckweed Lemna minor L. Science of the Total Environment 388:78-89.

Ushakov VL, Alipov ED, Shcheglov VS, Beliaev IY. 2006. Peculiarities of non-thermal effects of microwaves in the frequency range of 51-52 GHz on E coli cells. Radiatsionnaia Biologiia, Radioecologiia 46:719-728.

Ushakov VL, Shcheglov VS, Beliaev IY, Harms-Ringdahl M. 1999. Combined effects of circularly polarized microwaves and ethidium bromide on E coli cells. Electro- & Magnetobiology 18:233-242.

van Rongen E, Croft R, Juutilainen J, Lagroye I, Miyakoshi J, Saunders R, et al. 2009. Effects of radiofrequency electromagnetic fields on the human nervous system. Journal of Toxicology Environmental Health B Crit Rev 12:572-597.

Veyret B, Bouthet C, Deschaux P, de Seze R, Geffard M, Joussot-Dubien J, et al. 1991. Antibody responses of mice exposed to low-power microwaves under combined, pulse-and-amplitude modulation. Bioelectromagnetics 12:47-56.

Vilenskaya RL, Smolyanskaya AZ, Adamenko VG, Buldasheva ZN, Gelvitch EA, Golant MB, et al. 1972. Induction of the lethal colicin synthesis in E coli K12 C600 .E1. by means the millimeter radiation. In Russian. Bull Eksperim Biol Med 4:52-54.

Webb SJ. 1979. Factors affecting the induction of Lambda prophages by millimetre waves. Physics Letters 73A:145-148.

Yang Y, Jin X, Yan C, Tian Y, Tang J, Shen X. 2008. Case-only study of interactions between DNA repair genes .hMLH1, APEX1, MGMT, XRCC1 and XPD. and low-frequency electromagnetic fields in childhood acute leukemia. Leukemia & Lymphoma 49:2344-2350.

Yao K, Wu W, Yu Y, Zeng Q, He J, Lu D, et al. 2008. Effect of superposed electromagnetic noise on DNA damage of lens epithelial cells induced by microwave radiation. Investigative Ophthalmology & Visual Science 49:2009-2015.

Yao K, Wu W, Yu Y, Zeng Q, He J, Lu D, et al. 2009. Retraction. Effect of superposed electromagnetic noise on DNA damage of lens epithelial cells induced by microwave radiation. Investigative Ophthalmology & Visual Science 50:4530.

Zhao TY, Zou SP, Knapp PE. 2007. Exposure to cell phone radiation up-regulates apoptosis genes in primary culturese of neurons and astrocytes. Neuroscience Letters 412:34-38.

Zmyślony M, Politanski P, Rajkowska E, Szymczak W, Jajte J. 2004. Acute exposure to 930 MHz CW electromagnetic radiation in vitro affects reactive oxygen species level in rat lymphocytes treated by iron ions. Bioelectromagnetics 25:324-328.

Zotti-Martelli L, Peccatori M, Maggini V, Ballardin M, Barale R. 2005. Individual responsiveness to induction of micronuclei in human lymphocytes after exposure in vitro to 18