New biological studies on RF

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Inclusion

This presentation
reviews papers published in the last four years
and dealing with *in vivo* and *in vitro* effects of RF exposure
and lists the principal reviews issued on the subject

Exclusion

Some articles have been excluded for lack of proper dosimetry/exposure system description

Previous documents and statments

- Lyon, France – 2013. **Non-ionizing radiation, Part II**: Radiofrequency electromagnetic fields / IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. IARC monographs on the evaluation of carcinogenic risks to humans; **v. 102, 2013**

- **Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR).** Preliminary opinion on Potential health effects of exposure to electromagnetic fields. **December 2013**

European Commission

IARC Monograph - 2013

Cancer in humans

There *is limited evidence* in humans for the carcinogenicity of radiofrequency radiation. Positive associations have been observed between exposure to radiofrequency radiation from wireless phones and glioma, and acoustic neuroma.

Cancer in experimental animals

There is *limited evidence* in experimental animals for the carcinogenicity of radiofrequency radiation

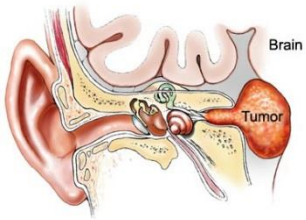
Overall evaluation

Radiofrequency electromagnetic fields are **possibly carcinogenic to humans** (group **2B**)

Rationale

Human epidemiological evidence was mixed: several small case-control studies uninformative, a large cohort study affected by lack of information. Interphone study and a study from Sweden showed an association in people with high use of mobile phone; inconsistencies between the two studies led to *limited evidence.* There was, however, a minority opinion that current evidence in humans was *inadequate.*

Acoustic neuroma



SCENIHR – December 2013

- The **exposure paradigm** of the general public has been changing in the last decades, anyway portable wireless telecommunication terminals are still the most frequent sources of human exposure. The introduction of new technologies is not expected to substantially raise the average levels of RF EMF in the environment.
- Due to the different frequencies used by the sources next to the body, it is important to take into account **multiple sources**, to combine exposure for risk assessment, as well as to calculate organ-specific doses, when possible
- **Epidemiological studies** on RF exposure do not unequivocally indicate an increased risk of brain tumors, and do not indicate an increased risk for other cancers of the head and neck region, or other malignant diseases including childhood cancer; the possibility of an association of RF exposure with acoustic neuroma remains open
- The earlier described evidence that RF exposure may affect **brain activities** as reflected by EEG studies during the wake and sleep state is further substantiated by more recent studies. The biological significance of the small physiological changes remains unclear.
- Overall, there is evidence that exposure to RF does not cause **symptoms** or affect **cognitive** function in humans.
- The previous opinion concluded that there were no adverse effects **on reproduction and development** from RF at exposure levels below existing limits. The inclusion of more recent human and animal data does not change that assessment

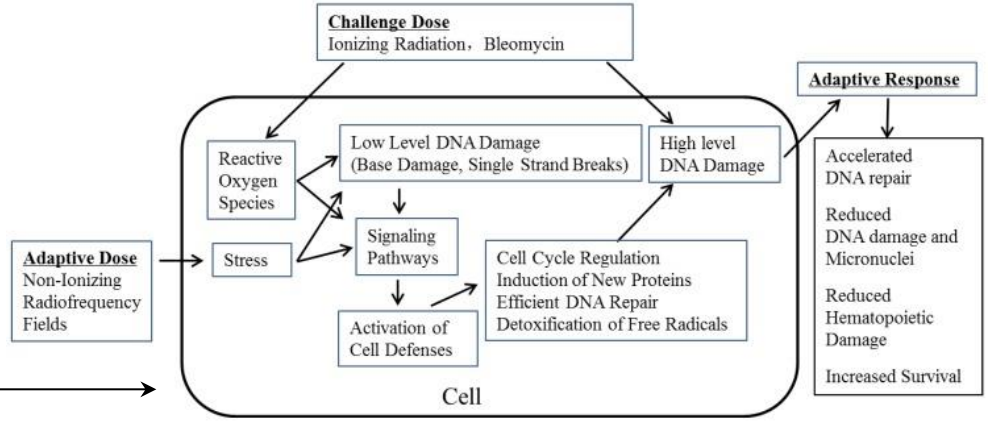
REVIEWS

Biological Effects of Radiofrequency Electromagnetic Field
Lai H, in Encyclopedia of Biomaterials and Biomedical Engineering. Taylor and Francis: New York, Published online: 12 Feb 2013; 1-8.

Effects of Radiofrequency-Modulated Electromagnetic Fields on Proteome
Leszczynski D, Radiation Proteomics, Advances in Experimental Medicine and Biology 990, 2013

A review of the ecological effects of radiofrequency electromagnetic fields (RF-EMF)
Cucurachi et al, Environment International 51, 116-140, 2013

Adaptive Response in Animals Exposed to Non-Ionizing Radiofrequency Fields: Some Underlying Mechanisms
Cao and Tong, Int. J. Environ. Res. Public Health 11, 2014



Searching for the Perfect Wave: The Effect of Radiofrequency Electromagnetic Fields on Cells
Gherardini et al, Int. J. Mol. Sci. 15, 5366-5387, 2014

International and National Expert Group Evaluations: Biological/Health Effects of Radiofrequency Fields
Vijayalaxmi and Scarfì, Int. J. Environ. Res. Public Health, 11, 9376-9408, 2014

REVIEWS

New horizons in enhancing the proliferation and differentiation of neural stem cells using stimulatory effects of the short time exposure to radiofrequency fields
Eghlidospour et al, J. Biomed. Phys. Eng, 5(3), 95-104, 2015

Anthropogenic radiofrequency electromagnetic fields as an emerging threat to wildlife orientation
Balmori A, Science of the Total Environment 518/519, 58-60, 2015

Effects of Cell Phone EMF Radiations on the Auditory System
Dabholkar et al, Int J Health Sci & Res 6(1), 506-515, 2016

The role of electromagnetic fields in neurological disorders
Terzi et al, Journal of Chemical Neuroanatomy, in press

Table 1 Auditory effects of Cell Phone

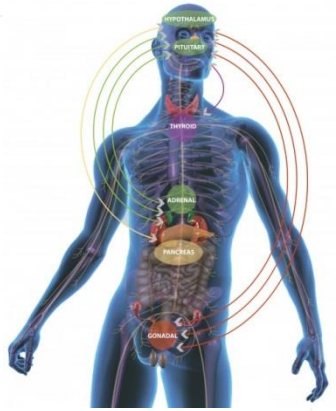
Investigators	Sample size	Findings
OktayMF,Dasdag F [28] (2006) Retrospective cohort.	60; 20 (2hr/day for 4 years), 20(10-20 minutes for 4 years) and 20 (never used cell phone	A higher degree of hearing loss is associated with long term exposure to EMF generated by cell phone.
Panda NK, et al [30] (2010) Retrospective, cross-sectional, randomized, case control study	112 cases using mobile phones >1 year. 50 controls that never used mobile phones.	High-frequency loss and absent DPOAE were observed with an increase in the duration of mobile phone use, excessive use of mobile phones.
C S Ramya, et al [35] (2011) comparative study	50 cell users for > 5 years. 25 <30min/day 25 >30min/day	Significant increase in the hearing threshold in mobile phone users associated with duration of usage.
S Bhagat, S Varshney, et al [33] (2012) Cohort study	75 cell users for > 4 years 2 Groups (<60 min and > 60 min) Also comparison between dominant and non-dominant ear	Prolonged, frequent exposure to EMFs from mobile phones does not cause damage to the inner ear as measured by DPOAE.
Mahesh Chandra Hegde, et al [36] (2013) Prospective study over 3 years	120 users. Group I >1hour for > than 1 year& Group II < 1 hour for < than a year or no usage	No significant difference in the 2 groups but minimal hearing loss of 5-15 dB in those exposed to mobile phone usage of more than 2 hours per day.
Hitesh Patel, Rizwan Qureshi(2013) [37] Retrospective	30 subjects > 1hour per day 30 subjects< 15 mins per day.	Some hearing impairment in long term mobile phone users compared to infrequent users. The dominant ear was affected more than non-dominant ear.
ShilpaKhullar , Archana Sood , Sanjay Sood (2013) [38] Retrospective	60 subjects;20 who never used cell phones,20 men who used for 10–20 min/day for 4 years and 20 men who used frequently (2 hrs. per day for 4 years)	Long term exposure to mobile phones may affect conduction in the peripheral portion of the auditory pathway.
P.Velayutham [39], et al (2014) Prospective single blinded study	100 subjects. Dominant ear (study group) compared to non-dominant ear (control)	High frequency hearing loss in the dominant ear (mobile phone used) compared to the non-dominant ear.

EHC / ICNIRP Review

1° step untill december 2012

2° step revision untill 2014/2015

Neuroendocrine System



10 GHz, 0.014 W/kg w.b., 2 h/day, 45 days *Kumar et al, Electromagn Biol Med, 31(3):223-232, 2012*	↑ serum melatonin	Wistar rats
10 GHz, 0.014 W/kg w.b., 2 h/day, 45 days *Kumar et al, Int J Radiat Biol, 89(3):147-154, 2013*	↓ serum testosterone level	Wistar rats
1800 MHz, 0.58 W/kg w.b., 2 h/day, 32 days *Qin et al, J Toxicol Environ Health A, 75(18):1120-1128, 2012*	↓ plasma melatonin	Sprague Dawley rats
905 MHz, 1.67 W/kg w.b., 2 h *Khirazova et al, Bull Exp Biol Med, 153(6):816-819, 2012*	**CHANGE** corticosteroids plasma level	Male and female rats
CDMA 849 MHz and WCDMA 1.95 GHz, whole body 2 W/kg, 45 min/day, 5 days/week up to 8 weeks *Jin et al, J Radiat Res, 54(3):430-437, 2013*	**NO** affect endocrine system (serum level of melatonin, TSH, T3, T4, ACTH and sex hormones)	Sprague Dawley rats
1800 MHz, 0.1 W/m^2, 40 min/day, 18 days *Pawlak et al, Int J Occup Med Environ Health 27(1), 114-122, 2014*	**CHANGE** thyroid hormones and corticosterone	Chickens' blood
1.8 GHz GSM, 2 W/kg, 24 h *Valbonesi et al, Int J Radiat Biol, 92(1),1-10, 2016*	↑ AChE but not gene and protein	Rat PC12 cells
900 MHz GSM, 6 W/kg in brain, 15 min *Bouji et al, Exp Gerontol, 47(6), 444-451, 2012*	↑ plasma corticosterone	Young, not in old Sprague Dawley rats

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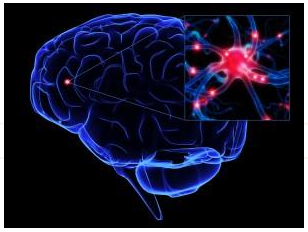

Nervous System and Behavior

918 MHz GSM, 0.25-1 W/kg, 2h/day, 12 or 60 days *Arendash et al, PlosOne 7(4): e35751, 2012*	reverses β-amyloid deposition modifies cerebral blood flow provides selected cognitive benefit in Alzheimer transgenic mouse model	>22 months old mice
Whole body exposure to 2.4 GHz WIFI signals, 1,6 W/kg, 1 month *Banaceur et al, Behav Brain Res 240, 197-201, 2013*	↑ Cognitive behavior	3xTg-AD mice
900, 1800 or 2450 MHz, 6x10^{-4} W/kg, 2 h/day, 5 d/week, 30 days *Desmuk et al, Toxicol Int 20(1), 19-24, 2013*	↑ DNA damage (comet assay)	Fisher 344 rat brain
900 MHz, 2 W/kg , 3h/day, 14 or 28 days *Tang et al, Brain Res 1601, 92-101, 2015*	↑ mkp-1/ERK pathway blood-brain barrier damage cognitive impairment	Rats
WiFi 2.4 GHz, 1-4 W/kg, 24h/day, 12 months *Dasdag et al, Int J Radiat Biol.; 91(7), 555-61, 2015;*	**CHANGE** expression of different miRNAs	Wistar rats brain
900 MHz, 0,12 W/kg, 3 h/day, 7 d/week, for 12 months *Dasdag et al, Int J Rad Biol 91(4),306-11, 2015*	**CHANGE** expression of rno-miR107 miRNA	Wistar rats brain
WiFi 2.4 GHz, 2,4 mW/kg local, 24 h/d, 12 months *Dasdag et al, Electromagn Biol Med 34(1), 37-42, 2015*	**CHANGE** cellular and anatomical parameters	Wistar rat testes

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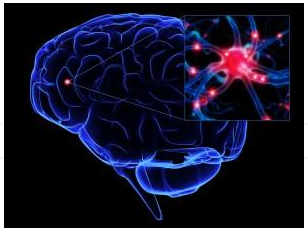


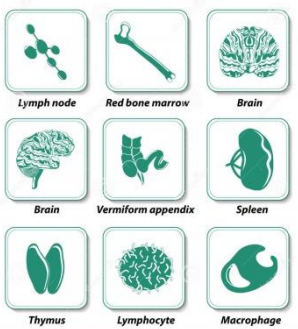
ICNIRP 8th INTERNATIONAL NIR WORKSHOP

Cape Town, South Africa, 9-11 May 2016

Nervous System and Behavior

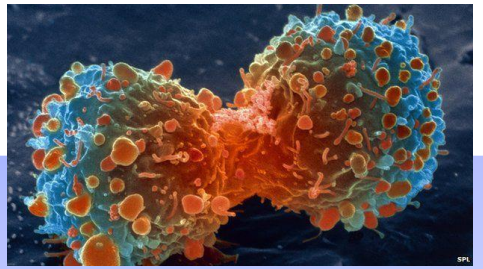
835 MHz, 4.0 W/kg, 5 hours/day for 4 and 12 weeks *Kim et al, PlosOne in press, 1-16, 2016*	↑ autophagy	Male, 6-week-old C57BL/6 mouse brain
1457 MHz, 50 min, 2.0 W/kg *Masuda et al, In Vivo 29(3), 351-7, 2015*	**NO** dynamic changes in BBB permeability	Young rats
2.856 GHz, 1.5 to 9 W/kg, 6 minutes, 3 times/week,6 weeks *Li et al, Physiol Behav, 140, 236-246, 2015*	↑ dose-dependent deficit of spatial learning memory accompanied with inhibition of brain electrical activity degeneration of hippocampus neurons disturbance of neurotransmitters	Male Wistar rats
1.800 GHz GSM, 3.2 W/kg *Moretti et al, Bioelectromagnetics 34(8), 571-8, 2013*	↓ spontaneous spiking activity and bursting rate during 3 min of exposure	Primary neuronal cell cultures from the cerebral cortex of embryonic rats.
1800 MHz, 1, 2, or 4 W/kg, 1, 2, or 3 days (intermittent mode) 5 min on/10 min off cycles *Chen et al. Sci Rep. 29(4), 5103, 2014*	↓ neurite outgrowth	Embryonic mouse neural stem cells
2.856 GHz (500 ns pulse width, 500 pps), 50 mW/cm^2, 5 min *Wang et al. Mol Neurobiol, 52(1), 478-91, 2015*	↑ structural damage ↑ permeability ↑ membrane/junction proteins pathways	*In vitro* blood–brain barrier model (ECV304 cell line co-cultured with primary rat cerebral astrocytes)

Immune System and Hematology



900 MHz, 0,5 W/kg (approx), 2h/day, 45 days *Sekeroglu et al, Int J Rad Biol 89(11), 985–992, 2013*	↑ chromosome aberrations (CA) micronucleus (MN) frequency, mitotic index (MI) ratio	Rat bone marrow cells
1800 MHz GSM, 2 W/kg, 1-24 h (5 min on, 10 min off) *Lu et al, PLoS One, e108318, 2014*	↑ pro-inflammatory responses	Mouse microglia (N9) but not astrocytes (C8-D1A) involving differential activation of STAT3
1457 MHz, 50 min, 2.0 W/kg *Masuda et al, In Vivo 29(5), 561-7, 2015*	**NO** change in hemodynamic parameters leukocyte adhesion to endothelial cells	Young rats
2.14-GHz W-CDMA, 0.2 W/kg w.b., 20 h/day, 7 d/week, 9 weeks spanning in utero development, lactation and the juvenile period in rats *Ohtani et al, J Rad Res 56(3), 467–474, 2015*	**NO** change on immune-like T cell populations, T cell activation, or Th1/Th2 balance although significant transcriptional effects were observed	
2.45-GHz, 2 and 10 W/kg, 4 and 24 h *Koyama et al. J Rad Res 56, 30–36, 2015*	**NO** effect on chemotaxis and phagocytosis	Human neutrophils

Cancer



Whole-body UMTS, 0.04, 0.4 and 2 W/kg
72 weeks starting in utero
at 14th day of pregnancy

↑ lymphomas, lung and liver tumors
without dose-response trend

ENU-treated mice

(Replication study)
Lerchl et al, Biochem Biophys Res Commun. 459(4), 585-90, 2015

1950-MHz (TD-SCDMA), 5 W/kg for 12, 24, and 48 h
Liu YX et al, BMC Public Health 15:764, 2015

NO effect on cell morphologies and ultra-structures
apoptosis, cell cycle progression,
tumor and apoptosis-related genes/proteins
tumor formation and invasiveness

in vivo in nude mice

NO effect on migration assays

in vitro in human glioblastoma cell lines

900 and 1800 MHz GSM EDGE, 2 W/kg, 1, 2, 3 and 4 h
(intermittent mode (15 min on/15 min off)

↑ proliferation (WST-1 assay)

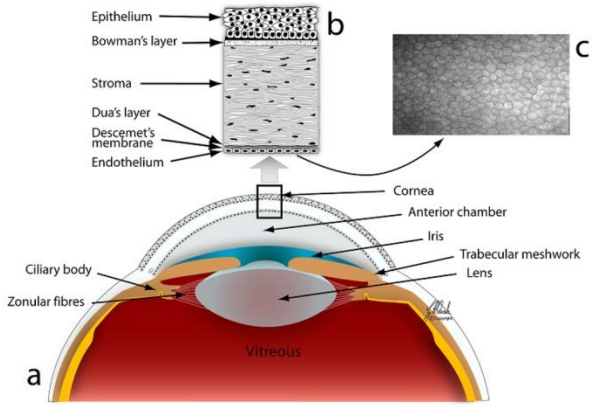
Human hepatocellular carcinoma cells

Ozgur et al. Cell Biochem Biophys 70(2), 983-91, 2014

Reproduction and Development

CDMA 849 MHz and WCDMA 1950 MHz combined **4.0 W/kg w.b., 45 min/d, 5 d/week, 12 weeks** *Lee et al, Bioelectromagnetics, 33, 356-364, 2012*	**NO** effect	Rat testicular function
WiFi 2450 MHz, 0.08, 0.4, 4 W/kg w.b., **2 h/day, 6 d/week, 18 days during pregnancy** *Poulletier de Gannes et al, Birth 1 Defects Res B Dev Reprod Toxicol, 95(2),130-136, 2012*	**NO** effect on implantation/foetus abnormalities physical and functional development	Newborns Wistar rats
WiFi 2450 MHz, 0.08, 0.4, 4 W/kg w.b. **1 h/day, 5 d/week, 16 days during pregnancy** *Aït-Aïssa et al, Bioelectromagnetics, 33(5), 410-420, 2012*	**NO** effect on pups number, body mass, genital abnormalities and antibodies production	Wistar rats
WiFi 2450 MHz, 0.08 or 4 W/kg w.b., **1 h/day, 3 weeks (males) or 2 weeks (females)** **+ 3 weeks during gestation** *Poulletier de Gannes et al , Reprod Toxicol, 36, 1-5, 2013*	**NO** effect on fertility, histology of reproductive organs and foetal abnormalities	Wistar rats
10 GHz, 0.014 W/kg w.b., 2 h/day, 45 days *Kumar et al, Int J Radiat Biol, 89(3):147-154, 2013*	↑ DNA damage and caspase-3 ↓ testosterone, testis weight and tubule diameter	Wistar rats
10 GHz, 0.014 W/kg w.b., 2 h/day, 45 days *Kumar et al, Electromagn Biol Med, 31(3), 223-232, 2012*	↓ serum melatonin level ↑ malondialdehyde/creatine kinase	Rat sperm cells
Multigenerational whole body exposure to 2.14 GHz, **< 0,24 W/kg, W-CDMA signals for 20 h/day** *Shirai et al, Bioelectromagnetics 35, 497-511, 2014*	**NO** adverse effects on F1/F2/F3 offspring	

Sensory Organs



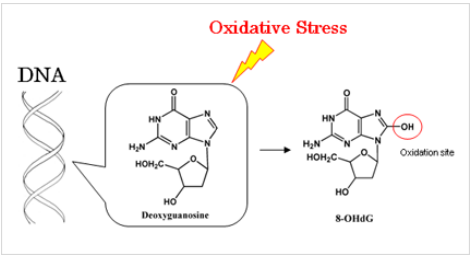
2.45 GHz, 2h/day, 21 days, 0,25 W/kg *Akar et al, Int J Radiat Bioll 89(4), 243-9, 2013*	↑ thickening of the anterior corneal epithelium	Male rats
1800 MHz GSM, 2, 3 or 4 W/kg, 0.5-24h *Ni et al, PlosOne 8 (8), 2013*	↑ ROS and lipid peroxidation ↓ gene/protein expression of antioxidant enzymes	Human lens epithelial (HLEB3) cells
GSM 900 MHz and1800 MHz and UMTS, 0.02, 0.2, 2, and 20 W/kg, 10 min (intermittent exposure) *Ahlers and Ammermuller, Bioelectromagnetics 35,16-29 2014*	**NO** effect under constant temperature conditions	Retinal ganglion cell responses

DNA Damage and oxidative Stress

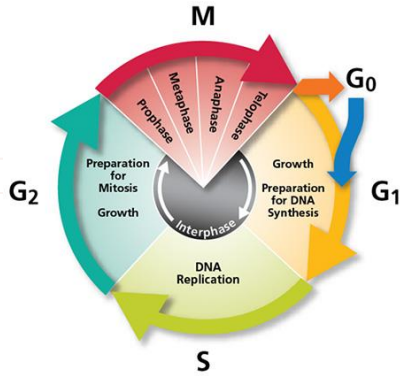
900 MHz, 0.01 W/kg w.b., 4 h/day, 45 days *Jelodar et al, Int J Radiat Biol. 89(2),128-31, 2013*	↑ biomarkers of oxidative stress	Rat's eye
900 MHz, 120 mW/cm^2 4 h/day, 7 days *Zong et al, Int J Radiat Biol. 91(3), 270-6, 2015*	↑ adaptive response ↓ BLM-induced DNA/oxidative damages	Adult mice
837 MHz and 1950 MHz alone or both, **4 W/kg single or 2+2 W/kg for both, 2 hours** *Hong et al. Bioel 33(7), 604-11, 2012*	**NO** effect on SOD activity, GSH/GSSG ratio ROS formation	Human MCF10A mammary epithelial cells
2.45 GHz, 0.023 W/kg w.b., 2 h/day, 45 days, **+ 5 days during mating** *Shahin et al, Appl Biochem Biotechnol, 169(5), 1727-1751, 2013*	↑ DNA damage in brain cells ↑ ROS levels, ↓ SOD/CAT/GPxin liver, kidney and ovary	Parkes mice
2450 MHz CW or WCDMA, 10 W/kg, 2 hours *Vijayalaxmi et al, Bioelectromagnetics 34(7), 542-8, 2013*	**NO** effect on micronuclei induction	Human peripheral blood lymphocytes
1800 MHz, CW, 1.3 W/kg, 24 h **(5 min on/10 min off cycles)** *Speit et al, Mutation Research 755,163–166, 2013*	**NO** effect on micronuclei frequency and DNA migration	HL-60 cells (replication study)
GSM 1800 MHz, 3.0 W/kg for 1 h or 24 h *Xu et al, PlosOne 8 (1), 2013*	↑ γH2AX foci formation **NO** effect in DNA fragmentation, cell cycle arrest cell proliferation or viability change	Chinese hamster lung cells and Human skin fibroblasts
1.800 GHz GSM, 0.2, 2 or 10 W/kg, 28 h **(5 min on/10 min off cycles),** *Waldmann et al. Radiat Res 179(2), 243-53, 2013*	**NO** effect on micronuclei	Human blood peripheral lymphocytes

DNA Damage and oxidative Stress

1800 MHz GSM , 1, 2 and 4 W/kg , 24 h (5 min on/10 min off cycles) *Liu et al, Toxicol Lett, 218(1), 2-9, 2013*	↑ SAR-dependent ROS generation and DNA adduct 8-oxoG	Mouse spermatocyte-derived (GC-2) cells
837 MHz CDMA + 1950 MHz WCDMA 2 W/kg, 2 hours, *Kang et al, J Radiat Res, 55(2), 265-76, 2014*	↑ ROS level 6 h post exposure ↑ ROS 12 h post exposure **NO** effect	U87 cells PC12 cells SH-SY5Y cells
940 MHz, 0.09 W/kg, 5-45 min *Sefidbakht Y et al, Photochem Photobiol Sci13(7), 1082-1092, 2014*	↑ ROS level	Human embryonic kidney cells (HEK293T)
10 MHz, 10 mT, 8h *Castello et al, Bioelectromagnetics 35, 598-602, 2014*	↓ proliferation and ↑ H_2O_2 production	Fibrosarcoma cell line
1950 MHz, 0.3 W/kg, 20 h *Sannino et al, Journal of Radiation Research 55, 210–217, 2014*	↑ adaptive response ↓ micronuclei incidence	Human peripheral blood lymphocytes treated with 1-1.5 Gy X-rays
1800 MHz GSM , 1, 2 and 4 W/kg , 24 h (5 min on/10 min off cycles) *Liu et al, Electromagn Biol Med. 34(1), 85-92, 2015*	↑ ROS and late-apoptotic cells	Mouse embryonic fibroblasts (NIH/3T3)
1800 MHz GSM, 2 W/kg, 0.5-8 hours *Hou et al, Electromagnetic biology and medicine 34, 85-92, 2015*	↑ ROS and % of late-apoptotic cells **NO** DNA damage	Mouse embryonic fibroblasts (NIH/3T3)
1800 MHz, 4 W/kg, 24 hours *Duan et al., Radiat Res 183(3), 305-14, 2015*	**NO** DNA strand breaks (Comet assay) and c-H2AX foci formation	GC-2 cells



Proliferation, gene and protein expression, Apoptosis



1800 MHz GSM, 0.1 to 4 W/kg, 15 min *Sun et al. International journal of radiation biology 88, 239-244, 2012*	↑ EGFR clustering on cell membrane ↑ phosphorylated EGFR	Human amniotic (FL) cells
1800 MHz GSM, 0.1 to 4 W/kg, 15 min *Sun et al, Int J Radiat Biol., 89(5), 378-83, 2013*	↑ EGFR clustering inhibited by co-exposure to magnetic field (30 – 90 Hz, 2 µT)	FL cells
837 MHz and/or 1950 MHz , 2-4 W/kg, 2-4 hours *Kim et al. J Radiat Res, 53(2), 176-83, 2012*	**NO** effect on HSP protein	Human mammary (MCF10A) cells
900 MHz GSM, 0.24 W/kg, 24h *Terro et al, Toxicology 292, 136-144, 2012*	**CHANGE** autophagy-related protein expression	Cortical cells
1950 MHz UMTS, 10 W/kg, 24 hours *Zeni et al. Bioelectromagnetics 33, 497-507, 2012*	**NO** effect on apoptosis (Annexin-V-FITC-PI test)	PC12 rat neuronal cells
837 MHz +1950 MHz, 2+2 W/kg, 4 hours or 2h/day, 3 days *Kim et al, Journal of radiation research 53, 176-183, 2012*	**NO** effect on MAPK kinase phosphorilation	MCF10A cells
900 MHz GSM, 2 W/kg, 6 hours *Simon et al, International journal of cosmetic science 35, 27-34, 2013*	**NO** effect on apoptosis-related parameters (H&E staining and cleaved caspase-3 expression)	Pigmented and non-pigmented skin cells

Proliferation, gene and protein expression, apoptosis (2)

1.800 GHz GSM, 2 W/kg, 1 hour *Cervellati et al, Oxid. Med. Cell. Longev, Article ID: 280850, 2013*	**CHANGE** transcript expression of integrin subunits α1, α5 and β1 and estrogen receptor β (ER-β)	Human trophoblast cells HTR-8/SV neo
1800 MHz GSM, 2.0 W/kg, 24 h (5 min on/10 min off cycles) *Zhijian et al. Biochem Biophys Res Commun 433(1), 36-9, 2013*	**CHANGE** apoptosis-related protein expression	Human B lymphoblastoid HMy2-CIR cells
1800 MHz CW, 2-4 W/kg, 2 hours *Zang et al, Hum Exp Toxicol. 32(8), 797-806, 2013*	**CHANGE** expression of 8 different proteins (by mass spectrometry)	
GSM 900 MHz, 0.25, 1, 2, and 4 W/kg 24h *Bourthoumieu et al, Bioelectromagnetics 34,52-60, 2013*	**NO** effect in P53 expression/activation	Human amniotic cells
1800 MHz GSM , 1, 2 and 4 W/kg , 24 h (5 min on/10 min off cycles) *Liu et al, Toxicol Lett 228(3), 216-24, 2014*	**CHANGE** expression of LC3-I, LC3-II, p62 and p-ERK proteins	GC-2 cells
2.856 GHz, 10-100 mW/cm², 5 min *Zuo et al, Int J Med Sci 11, 426-435, 2014*	↑ apoptosis via mitochondrial-dependent caspase-3 pathway	PC12 cells

Proliferation, gene and protein expression, apoptosis (3)

60.4 GHz , 20 mW/cm^2, 3 hours *Habauzit et al, PLoS One, e109435, 2014*	**CHANGE** in microarray test in association with temperature increase	Primary human keratinocytes
1.8 GHz GSM-217Hz mod, 2 W/kg, 4-24 hours *Valbonesi et al, Int J Radiat Biol, 90(5), 382-91, 2014*	↑ HSP70 transcript expression (no effect of CW and talk-mode)	PC12 cells
60 GHz, 1-20 mW/cm^2, 20 min to 24 h *Le Quément et al, Bioelectromagnetics 35, 444-51, 2014*	**NO** effect on transcript expression of BiP and ORP150 effect on HSP due to thermal increase	Human malignant melanoma cell line (A375) and human keratinocyte cell line (HaCaT)
2.856 GHz, 4 W/kg, 6 min **(50 pulses/sec, pulse width 500 ns)** *Wang et al, PLoS One10(2):e0117550, 2015*	**NO** effect on cell cycle and proliferation	Primary murine bone marrow mesenchymal stem cells (BM-MSCs)
900 MHz CW, 2 and 20 W/kg, 90 min **and 1800 MHz, 2.5 and 12.4 W/kg, 120 min** *Kumar et al, Int J Radiat Biol 91(8), 664-72, 2015*	**NO** effect on proliferation	Rat lymphoblast
2.856 GHz, 4 W/kg, 6 min **(50 pulses/sec, pulse width 500 ns)** *Wang et al PloS one 10, e0117550, 2015*	**NO** effect on apoptosis (Annexin-V-FITC-PI test)	Primary murine bone marrow mesenchymal stem cells
1800 MHz GSM, 0.35 W/kg, 24 h *Canseven et al, Electromagnetic biology and medicine 34(4), 322-6, 2015*	↑ apoptosis (Annexin-V-FITC-PI test), ↓ viability	Burkitt's lymphoma (Raji) cells

Conclusion

- ✓ The literature from 2012 to 2016 still confirms the weak of experimental results according to unavailability of dose-response curves and the spread of the data in terms of SAR values, overall exposure time, etc.
- ✓ In presence of effects, ie at molecular level, they are not deeper investigated in order to identify a possible biological response at different level and to finalize the weight of the results.
- ✓ We still need a more accurate and systematic experimental approach able to suggest possible interaction mechanisms.