Evidence of genotoxic effects in isolated mammalian cells after exposure to cell phone radiation

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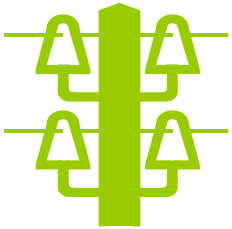
What does occur in isolated human cells after exposure to cell phone radiation below the safety limits ?

What are the conclusions we have to draw from the research results with regard to our health ?

Scientific approach

Exposure



50 Hz
Extremely low frequency (ELF) fields

900 MHz
1800 MHz
Radiofrequency (RF) fields
UMTS

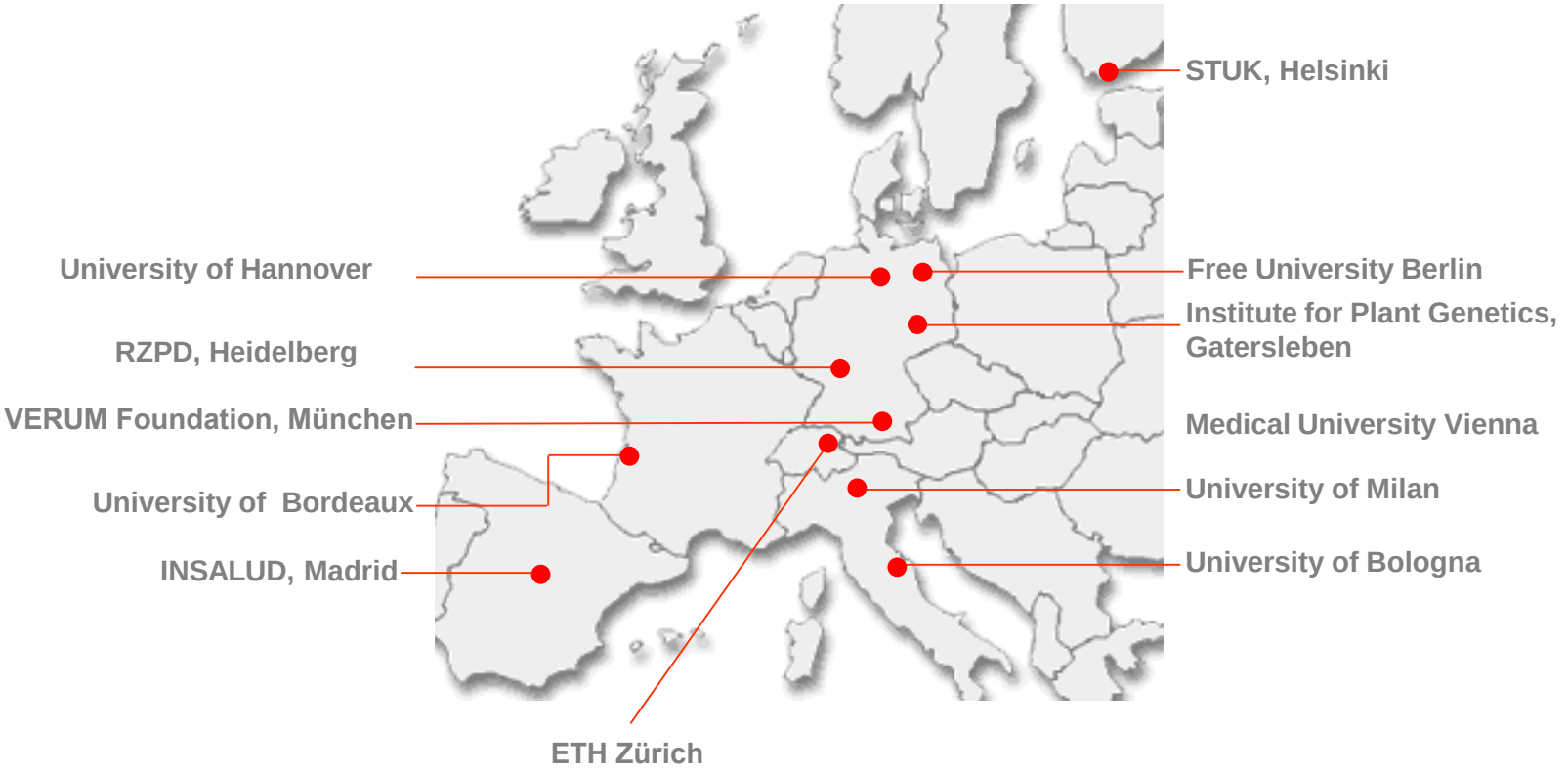
Search for Effects

Investigations

- Epidemiological studies
- Animal studies
- **Studies on cell and tissue culture**

Risk Evaluation of Potential Environmental Hazards From Low Energy Electromagnetic Field Exposure Using Sensitive *in vitro* Methods

A project funded by the European Union under the programme "Quality of Life and Management of Living Resources", Key Action 4 "Environment and Health": QLK4-CT-1999-01574



State-of-the-art in 1999

Even though the biological effects of electromagnetic field (EMF) exposure have been studied for the past 80 years, no consensus has been reached with respect to either findings or their interpretation.

The reasons for this are numerous:

- **difficulties in measuring EMF exposure at the putative sites of action**
- **vast differences in exposure and experimental conditions**
- **the complete lack of agreement on biological endpoints appropriate for study**

Assumption and aim of the study

REFLEX was based on the assumption that a health risk due to EMF below the current safety limits can only exist if scientific proof of biological effects, relevant for the development of diseases, is obtained.

The aim of REFLEX was to find out whether or not EMF below the current safety limits cause cellular, sub-cellular or molecular alterations in isolated mammalian cells that are relevant for the development of diseases.

Pathogenesis of chronic diseases

All chronic diseases such as cancer and neurodegenerative disorders are of extremely diverse and heterogeneous origin.

This variability is generated by alterations of the structure and function of the genes leading to changes in gene and protein expression.

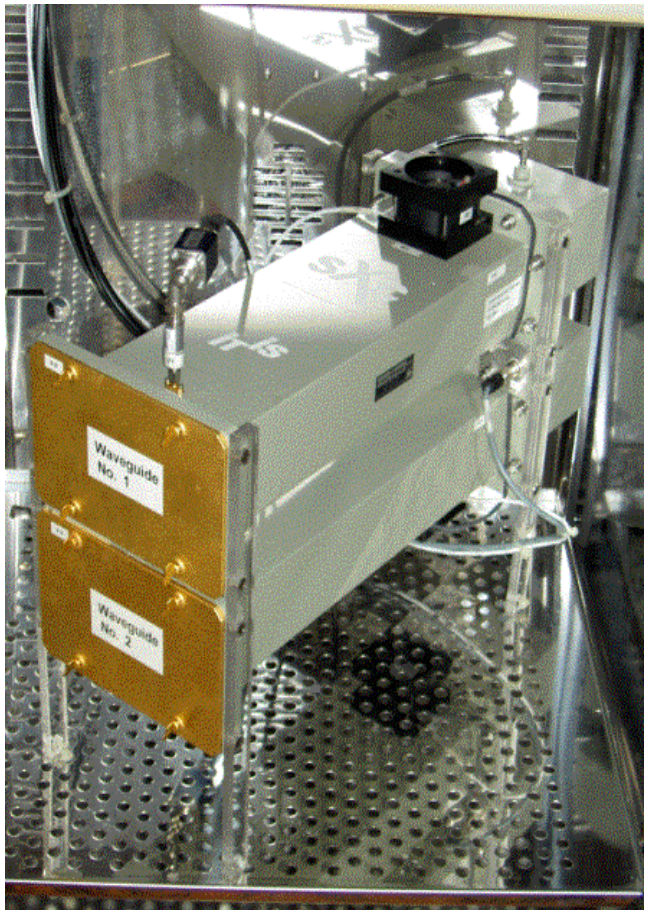
This may result in a number of critical cellular events, e. g.
- deregulated cell proliferation or cell differentiation
- suppressed or exaggerated programmed cell death (apoptosis)

The convergence of various critical events is required for the development of chronic diseases.

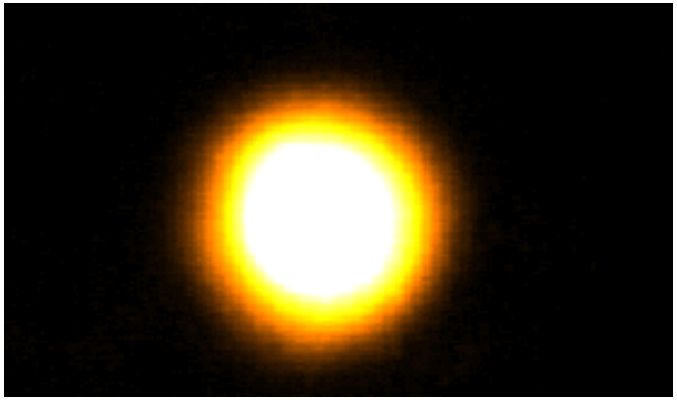
Working hypothesis to be tested in REFLEX

Our working hypothesis based on the state-of-the-art in 1999 assumed that no biologocal effects of relevance for the pathogenesis of chronic diseases will be detected and that the present safety limits reliably protect EMF-exposed people from any health risk.

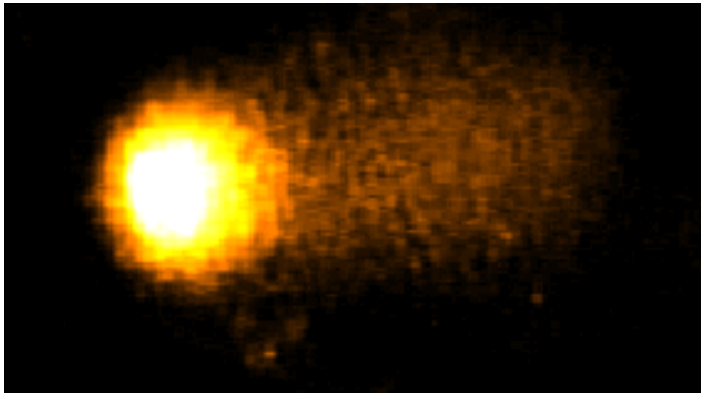
Exposure chamber



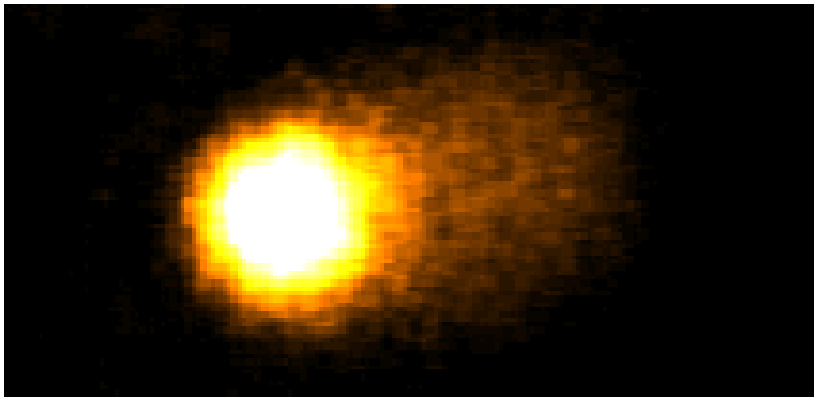
Comet assay



sham exposition

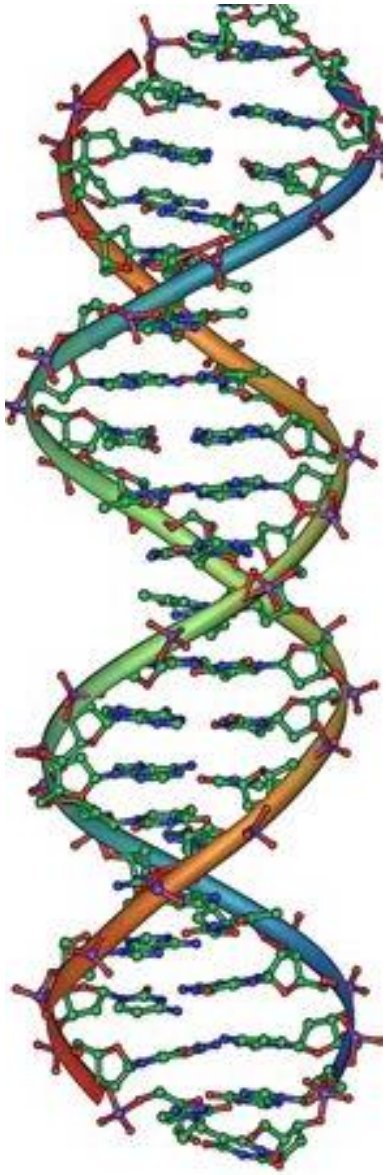


gamma-radiation; 0,5 Gy

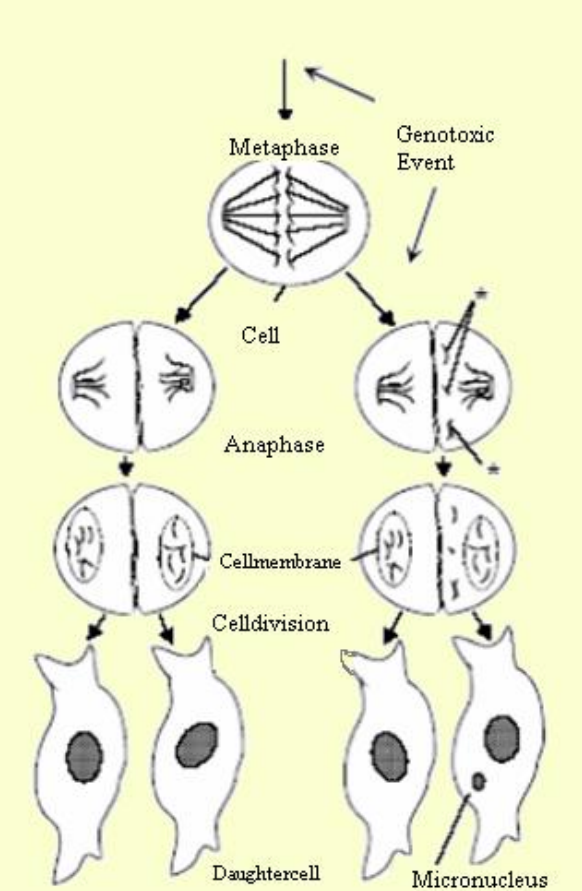


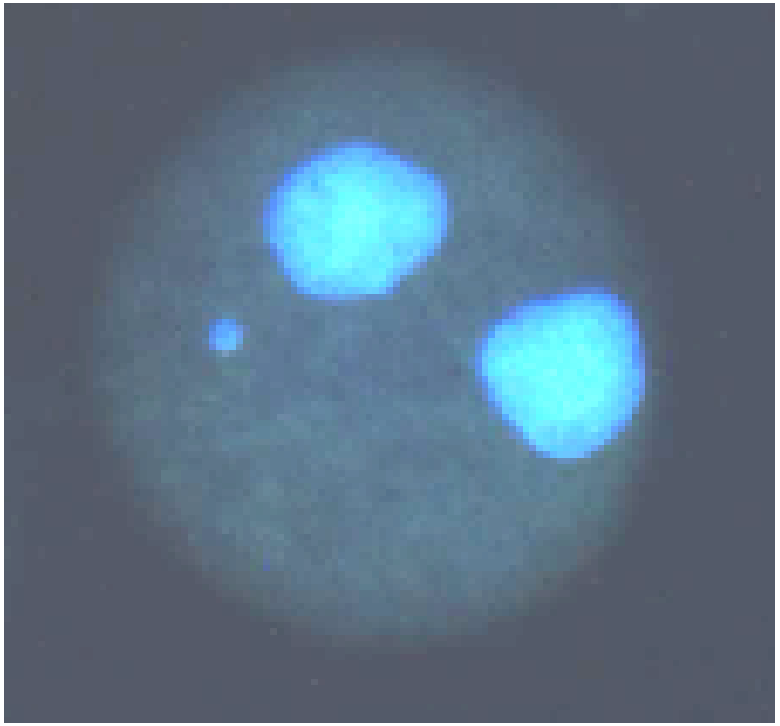
RF-EMF: 1800 MHz; SAR 1.3 W/kg; 24h

DNA structure



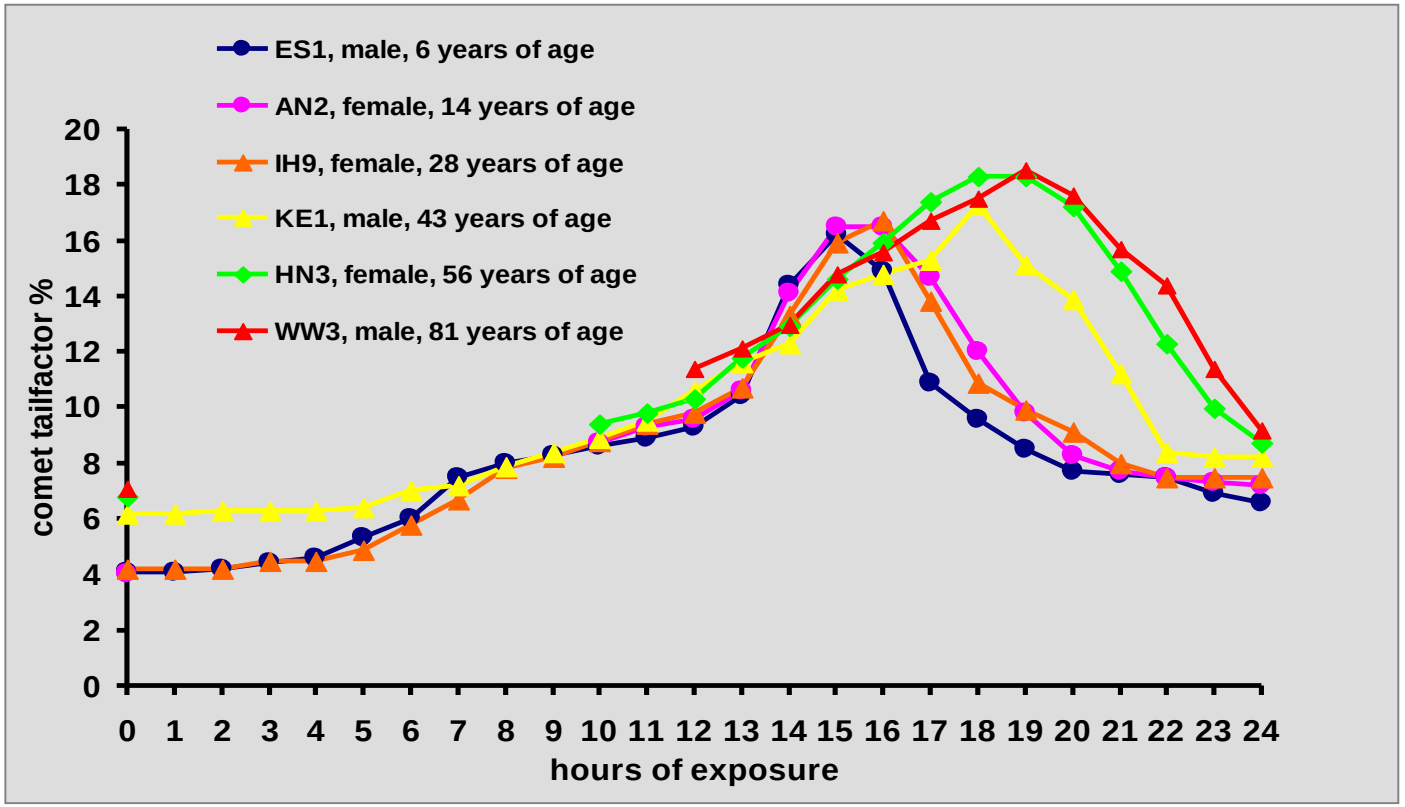
Micronucleus test





ELF-EMF _ Age-dependent increase of DNA strand breaks in human fibroblasts

50 Hz sinus; 1000 µT; 5 min on / 10 min off



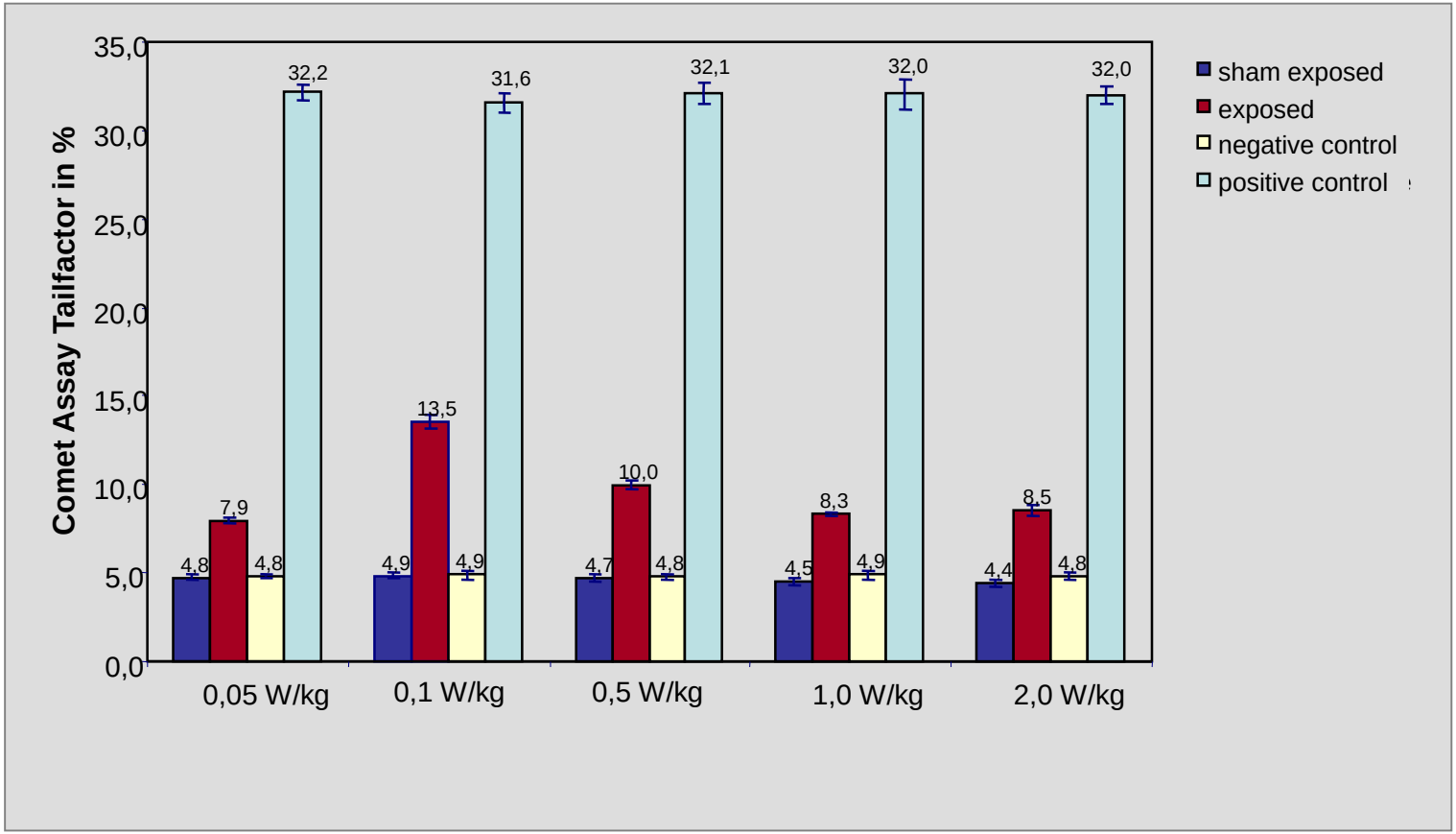
UMTS _ Dose dependency

- UMTS 1950 MHz
- normal human fibroblasts (cell line ES-1)
- exposure duration: 24 hours
- exposure pattern: continuous
- SAR values: 0.05 W/kg, 0.1 W/kg, 0.5 W/kg, 1.0 W/kg and 2.0 W/kg
- endpoints: comet assay, micronucleus test

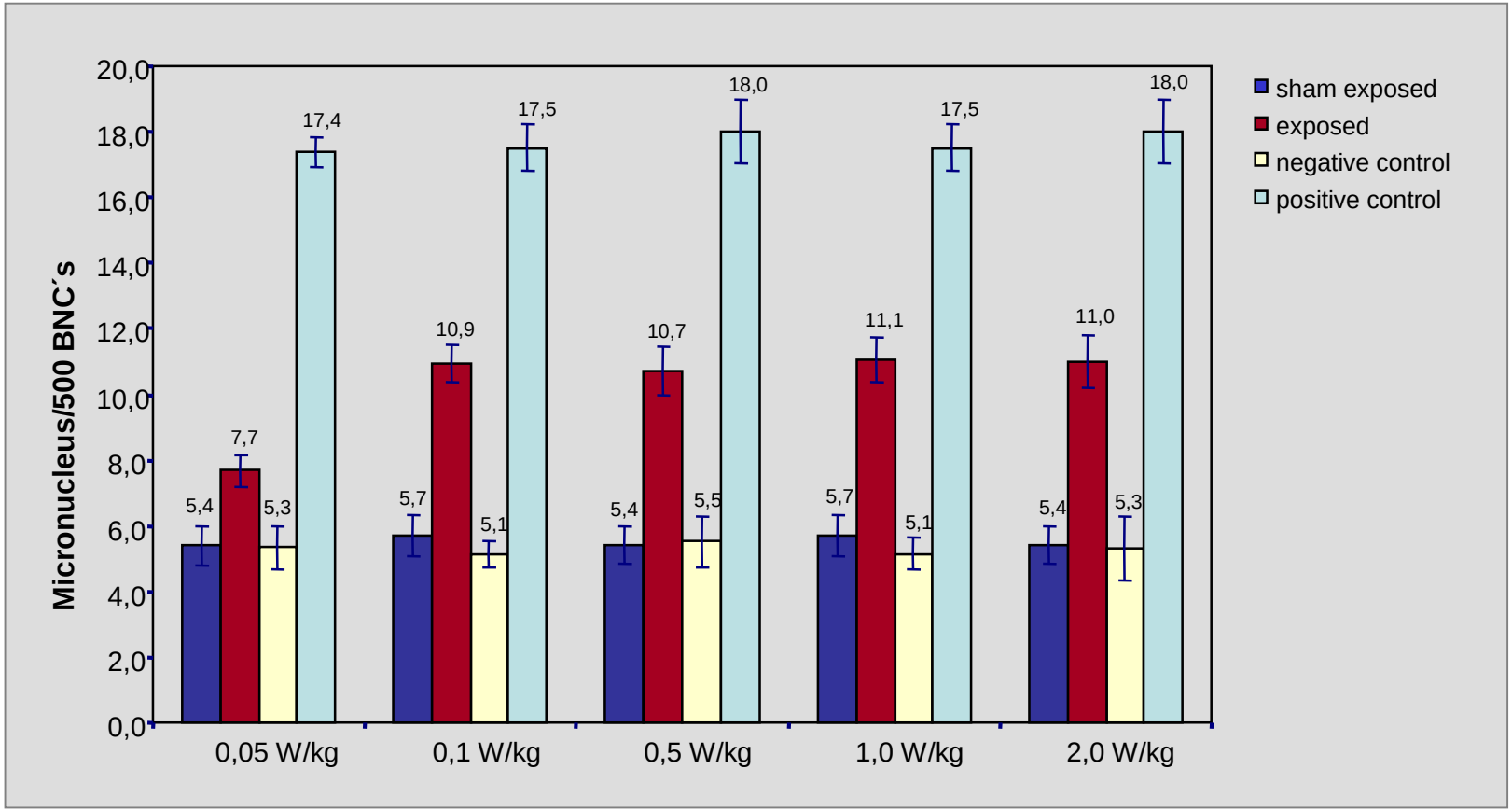
positive controls in the comet assay: UV light, 254 nm, 3 min, 800 µW/cm²

positive control in the micronucleus test: 25 nM Vincristin

Dose-dependent increase in DNA strand breaks after UMTS exposure



Dose-dependent increase of micronuclei after UMTS exposure



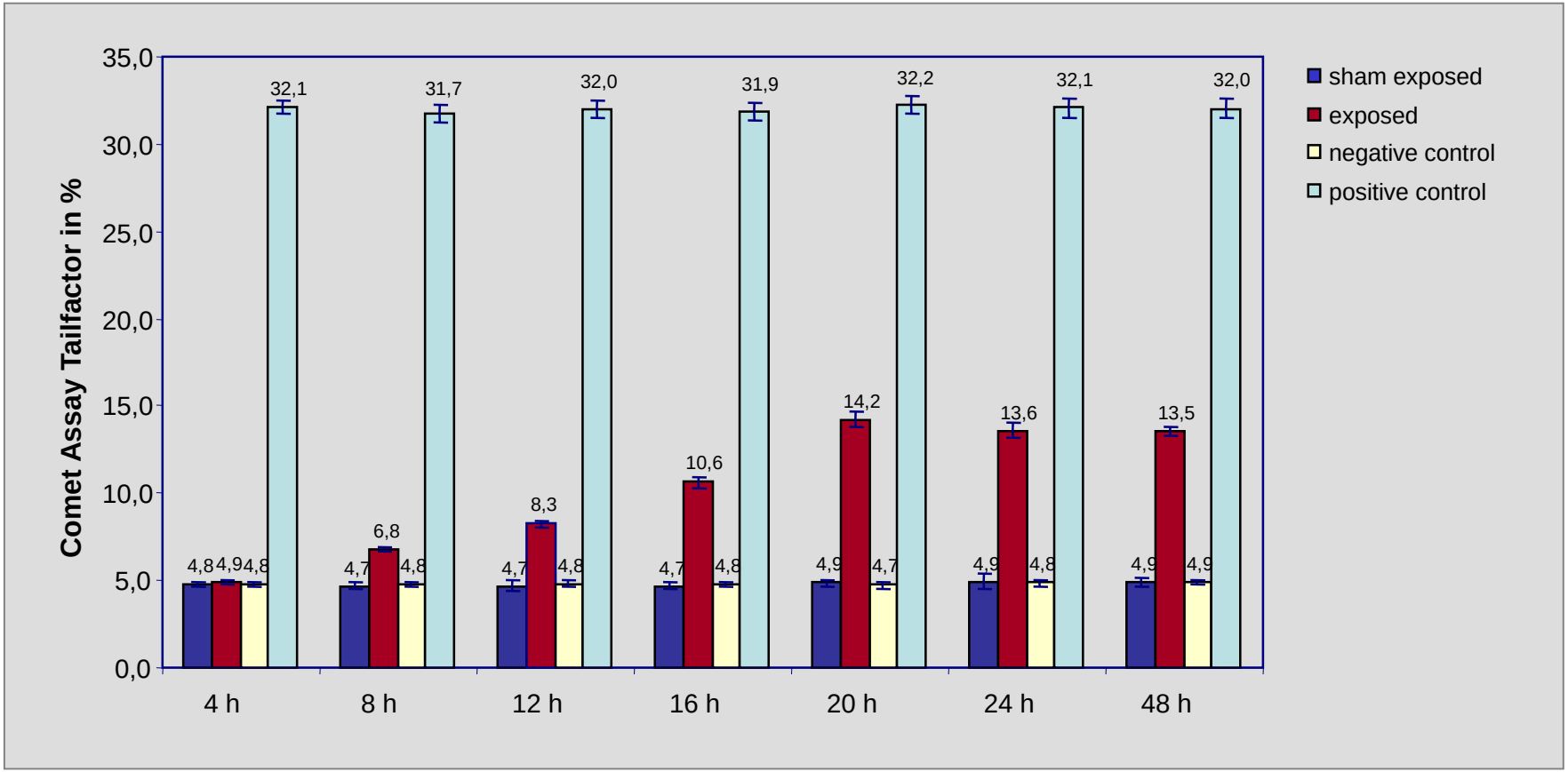
UMTS _ Time dependency

- UMTS 1950 MHz
- normal human fibroblasts (cell line ES-1)
- SAR value: 0.1 W/kg
- exposure pattern: continuous
- exposure duration: 4, 8, 12, 16, 20, 24 and 48 hours
- endpoints: comet assay, micronucleus test

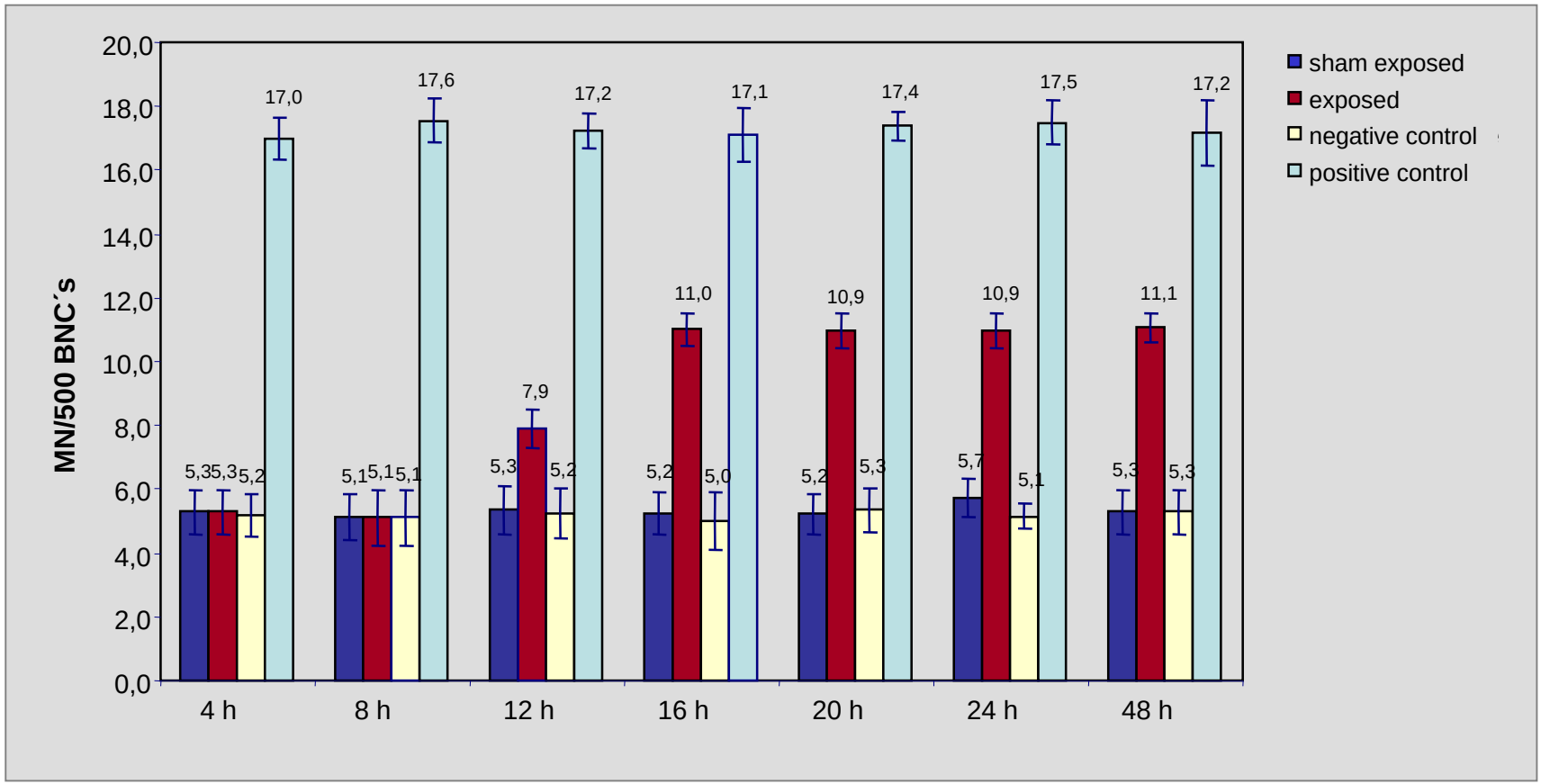
positive controls in the comet assay: UV light, 254 nm, 3 min, 800 µW/cm²

positive control in the micronucleus test: 25 nM Vincristin

Time-dependent increase of DNA strand breaks after UMTS exposure



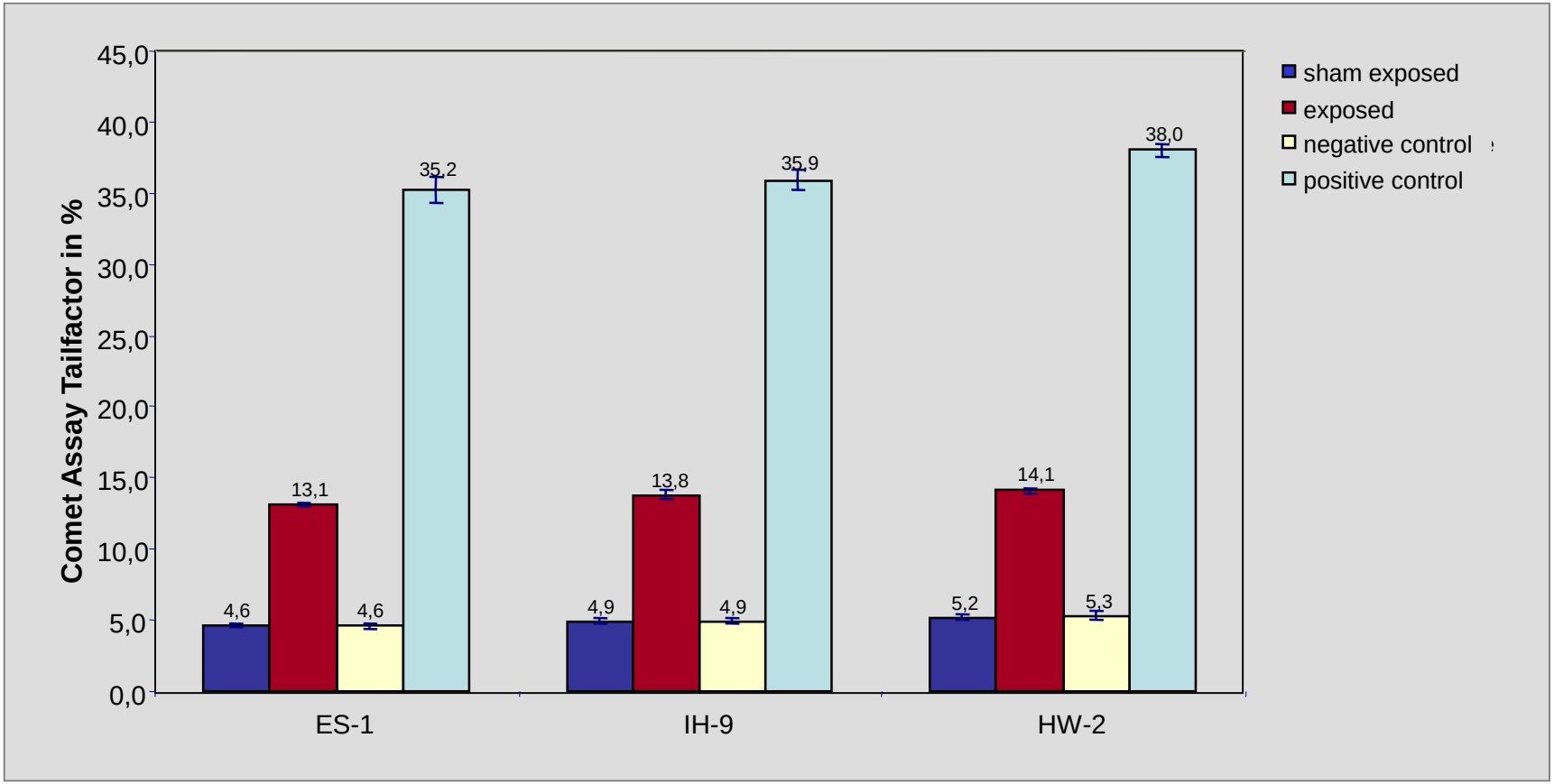
Time-dependent increase of micronuclei after UMTS exposure



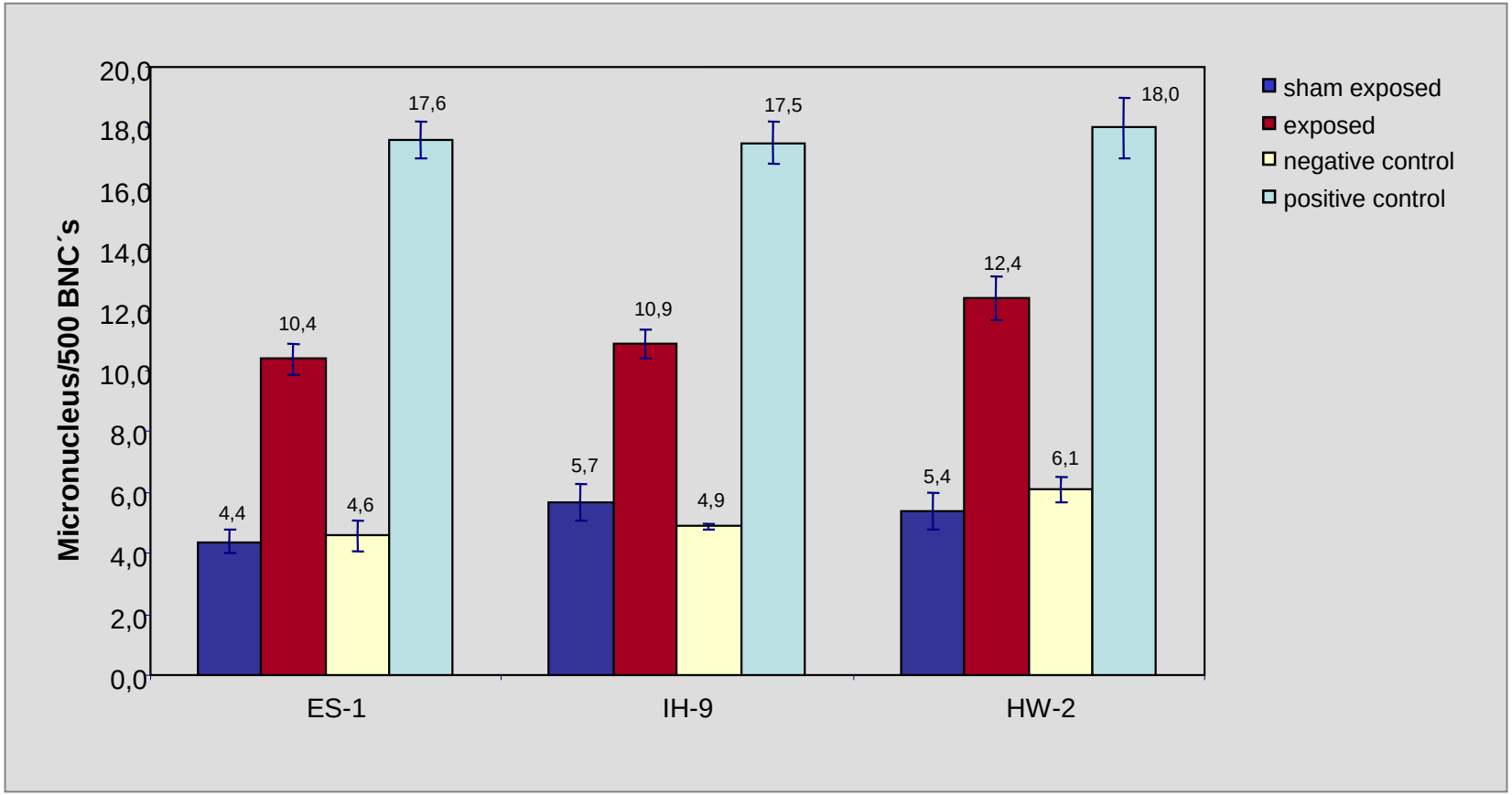
UMTS _ Repetition with 3 different cell lines

- UMTS 1950 MHz
- SAR value: 0.1 W/kg
- exposure duration: 16 hours
- exposure pattern: 5 mon on / 10 min off
- cells: 3 different cell lines from human fibroblasts

Increase of DNA strand breaks in fibroblasts from three different persons after UMTS exposure



Increase of micronuclei in fibroblasts from three different persons after UMTS exposure



RF-EMF _ Effects on gene and protein expression

GSM; 900 MHz; SAR 2 W/kg; 1h

After an 1-hour exposure at 2.0 W/kg

RF-EMF activated

- **gene expression (MAPK p38, PKC)**
- **protein expression (HSP27)**
- **cellular metabolism by protein phosphorylation (HSP27)**

from: Dariusz Leszczynski, Radiation and Nuclear Safety Authority (STUK), Finland

Summary of the REFLEX results

The results obtained in the REFLEX and its follow-up study did not confirm our original hypothesis of zero EMF effects.

ELF-EMF and RF-EMF far below the safety limits alter the structure and function of genes in different animal and human cells.

In more detail, we saw

- **an increase of single and double DNA strand breaks in human fibroblasts, HL60 cells and granulosa cells of rats, but not in human lymphocytes**
- **an increase of micronuclei and chromosome aberrations in human fibroblasts**
- **alterations in gene and protein expression of several cell types, especially in human fibroblasts, human endothelial cells and embryonic stem cells from mice**

Transient DNA damage induced by high-frequency electromagnetic fields in the human trophoblast HTR-8/SVneo cell line evaluated with the alkaline comet assay

One of the most controversial issue regarding high-frequency electromagnetic fields (HF-EMF) is their putative capacity to affect DNA integrity. This is of particular concern due to the increasing use of HF-EMF in communication technologies, including mobile phones. Although epidemiological studies report no detrimental effects on human health, the possible disturbance generated by HF-EMF on cell physiology remains controversial. In addition, the question remains as to whether cells are able to compensate their potential effects.Wehave previously reported that a 1-h exposure to amplitude-modulated 1.8GHz sinusoidal waves (GSM-217 Hz, SAR = 2 W/kg) largely used in mobile telephony did not cause increased levels of primary DNA damage in human trophoblast HTR-8/SVneo cells. Nevertheless, further investigations on trophoblast cell responses after exposure to GSM signals of different types and durations were considered of interest. In the present work, 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. However, alterations were rapidly recovered and the DNA integrity of HF-EMF exposed cells was similar to that of sham-exposed cells within 2 h of recovery in the absence irradiation. Our data suggest that HF-EMF with a carrier frequency and modulation scheme typical of the GSM signal may affect the DNA integrity.

Amplitude-modulated GSM signals at a SAR of 2.0 W/kg significantly increased the rate of DNA strand breaks in human trophoblasts after an exposure time of 16 and 24 hours. The conclusion is that HF-EMF with a carrier frequency and a modulation scheme typical of the GSM signal may affect the DNA integrity.

Franzellitti S et al.: Transient DNA damage induced by high-frequency electromagnetic fields (GSM 1.8 GHz) in the human trophoblast HTR-8/Svneo cell line evaluated with the alakline comet assay. Mutat Res. 2009 Oct 12. [Epub ahead of print]

Exposure to 1800 MHz radiofrequency radiation indueced oxidative damage to mitochondrial DNA in primary cultured neurons

Increasing evidence states that xidative stress may be involved in the adverse health effects of radiofrequency radiation (RF) on the brain. Since mitochondrail DNA (mtDNA) defects are closely related with various nervous system diseases and mtDNA is highly susceptible to oxidative stress, the purpose of this study was to determine whether radiofrequency radiation could cause oxidative damage to mtDNA. In this study, we exposed primary cultured cortical neurons to pulsed RF electromagnetic fields at a freqeuncy of 1800 MHz modulated by 217 Hz at an average special absorption rate (SAR) of 2 W/kg. At 24h after expposure, we found that RF radiation induced a significant increase in the levels of 8-hydroxyguanine (8-OHdG), a common biomarker of DNA oxidatic´ve damage, in the mitochondria of neurons. Consistent with this, the copy number of mtDNA and the levels of mitochondrial RNA (mtRNA) transcripts showed an obvious reduction after RF exposure. All these mtDNA distrurbances could be reversed by pretreatment of melatonin, an effective antioxidant in brain. Together, these results suggested that 1800 MHz RF radiation could cause oxidative damage to mtDNA in primary cultured neurons. Oxidative damage to mtDNA may account for the neurotoxicity of RF radiation in the brain.

A research group from China exposed primary cultured cortical neurons to GSM signal-like radiation at a SAR of 2 W/kg for 24 hours. They observed a significant increase in the reactive oxygen species (ROS) production and, in addition, also a significant rise of 8-OHdG in the mitochondrial DNA of the neurons. 8-OHdG are typical DNA adducts generated under stress through free radicals.

Xu S et al. (2009) Exposure to 1800 MHz radiofrequency radiation induced oxidative damage to mitochondrial DNA in primary cultured neurons. Brain Res. 2009 Oct 29 [Epub ahead of print]

RF-EMF _ Contribution to pathogenesis

875 MHz; SAR < 2 W/kg; minutes

Step 1 Activation of NADH oxidase in the cell membrane

- NADH oxidase → ROS ⇢ DNA damage?

Step 2 Activation

- Matrix metalloproteinase → Hb-EGF

Step 3 Activation

- ERK cascades → Cell proliferation
  Signal transduction
  Metabolism
  DNA repair
  Coping with stress

from: Friedman et al. (2007) Mechanisms of short-term ERK activation by electromagnetic fields at mobile phone frequencies. Biochem J 405: 559-568

EMF - a risk to our health?

None of the single approaches in

- **basic research**
- **animal experiments**
- **epidemiological studies**

is at present in the position to provide proof of a health risk caused by EMF with sufficient certainty.

However, the fact that the results from the three approaches complement each other strongly speaks in favour of the assumption that a health risk could arise from ELF-EMF as well as from RF-EMF.

Worst case scenario

Genotoxic alterations such as caused by mobile phone radiation are the basic events underlying cancer development.

This speaks in favour of a causality between the long-term use of mobile phones and the increase in the brain tumour risk as already observed in epidemiological studies.

Conclusions

The available scientific data clearly demonstrate that G2 and G3 radiation below the current safety limits are athermal by nature.

Since the current safety limits are based upon the assumption that athermal biological effects do not exist, the only possible conclusion is that they are not safe and do not protect our health.

To reduce the safety limits by a factor of up to a ten thousandth may be a first and easily to accomplish step to adjust radiation intensity to the conditions of the living organism.

The development of a new generation of safety limits away from thermal and towards biological EMF effects is a top priority, but can only be achieved by independent research.

The all-clear signal
from the industry and their scientific advisers denying any possible health risks of people exposed to radiofrequency EMF below the safety limits do not have a sound basis.

Therefore,
the national governments which are responsible for the health protection of their citizens are badly advised, if they back the current safety limits and with it also the all-clear signal of the industry.

The public has the right to hear at once about any new scientific information related to cell phone exposure and the conclusions drawn.

This is especially true, when research comes up with increasing suspicion that this kind of radiation may have a significant health impact.

Labelling cell phones with a warning message is probably one of the best ways to ensure public awareness, and it is a government task of great significance to enforce this by law before it is too late.