German Mobile Telecommunication Program

International Workshop

Action Mechanisms

May 9 - 10, 2007

Rapporteur's Report

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Session 1

Functional Aspects

Asmuß

(Chair)

Genotoxic Effects of HF-signals on Human Cells *in vitro*

D. Pollet
P. Waldmann

University of Applied Sciences
Darmstadt, Germany

German Mobile Telecommunication Program

Funding
Federal Office for Radiation Protection

RFR-exposure Equipment & Dosimetry
IT'IS, Zürich

Donor Recruitment, Blood Sampling, Exposures & Analyses
INCOS & IMBEI, University of Mainz

Genotoxicity Evaluation
Dermatology Center, Buxtehude (near Hamburg)
University of Applied Science, Darmstadt (near Frankfurt)
Cytotest Cell Research GmbH, Roßdorf (near Gottingen)

‘Blind’ Study

Peripheral Blood Donors

10 males - between 50 - 60 yrs
10 males - <18 years

RFR-exposure G_1, S & G_2 phases of cell cycle

Frequency 1800 MHz

SAR 0.0, 0.2, 2 & 10 W/kg

Exposure 24 hours

Genotoxicity End-points

Alkaline Comet Assay	100 cells / donor
Chromosomal Aberrations	1000 cells / donor
Micronuclei	2000 cells / donor
Sister Chromatid Exchanges	50 cells / donor

Project **On-Going**

Functional & Molecular Investigations after 1.8 GHz Radiofrequency Electromagnetic Fields Exposure in Different Immune Relevant Cells

M. Simko

University of Rostock
Rostock, Germany

The overall data suggested that GSM-DTX exposure at high peak SAR levels induced alterations in free radicals release & changes in protein expression levels

However, these alterations did not induce changes in physiological processes such as phagocytosis, cell proliferation, apoptosis & necrosis

Session 2

Gene Expression

Ziegelberger

(Chair)

Effects of HF-signals on the Melatonin Synthesis in isolated pineal organs of Djungarian Hamsters

A. Lerchl

Jacobs University
Bremen, Germany

The overall data indicated
no adverse effects in
the synthesis of melatonin
by the pineal gland
at SAR levels
which are relevant
to human exposure

Effects of Mobile Phone Signals (GSM & UMTS) on the Blood-Brain Barrier *in vitro*

H. Franke

University Hospital Munster, Department of Neurology
Munster, Germany

Isolated RNA from cells exposed to GSM (1800 MHz) and UMTS was subjected to genechip array and quantitative real time PCR analysis.

Compared with sham-exposed cells, the expression profiles of exposed cells revealed 1.5 to 3-fold changes in 13 genes in UMTS and 5 genes in GSM were significantly regulated at least at one SAR. These genes includes those encoding for proteins known for their relevance for proper BBB functions such as cellular differentiation, signal transduction, etc.

There was no SAR-dependent relationship.

Overall this study identified several candidate genes that showed differential expression due to “non-thermal” (less than +1 ℃ warming) influence of RF-EMF exposure. The data obtained here do not point towards any pathophysiologically relevant events in humans”

PANEL DISCUSSION

Do we need further studies on melatonin

Do the existing & currently running studies on possible effects of RF-EMF on B-B-B enough

Are screening arrays adequate to detect relevant markers / end-points

What are the limitations to interpret the results from screening arrays? What if certain changes do not lead to detectable effects *in vitro* and *in vivo*

Should further research be focused on certain molecular targets

If so – which are the relevant candidates

Session 3

Sensory Systems

Pophof

(Chair)

Effects of HF-signals on Retinal Ganglion Cell Activity

J. Ammermüller

Department of Neurobiology
University of Oldenburg, Germany

The overall data indicated that the response of
Isolated mouse retinal cells exposed
(inside a calibrated exposure system)
to GSM & UMTS signals (900 & 1800 MHz)
at 0.02, 0.2, 2.0 & 20 W/kg SAR
did not differ significantly/systematically
from sham-exposed cells

Temperature increase alone induced
increased response rate
decreased latency periods

The putative effects can result from
thermal warming
but not from
HF-EMF effects *per se*.

Ionic currents through Ca^{2+} channels in mature mouse inner hair cells under mobile phone field exposure

J. Engel

Universitat Tubingen
Tubingen, Germany

Patch-clamp recordings of the currents through Ca^{2+} channels were made in mature inner hair cells before, during & post-exposure to 1800 MHz GSM & UMTS 0.02, 0.2, 2.0 & 20 W/kg SAR.

No statistically significant effect was observed on Ca^{2+} channels

PANEL DISCUSSION

Is electrophysiology a reliable method to investigate possible action of EMF on sensory systems

Were the study design, number of replications & statistical analysis appropriate to achieve reliable results

What are the underlying mechanisms of the described effects

What is the thermal response threshold of sensory cells & neuronal network

What are the physiological & health consequences of the effects observed

Session 4

Action Mechanisms

Geschwentner

(Chair)

Dielectric Properties of Tissues & Cells

A. Loidl

Experimental Physics University of Augsburg
Augsburg, Germany

Broadband dielectric spectra were obtained in human peripheral whole blood & in different concentrations of cultured cells

(fibroblasts, melanoma cells, nerve cells & keratinocytes)

Detailed analyses indicated that even at GHz frequencies AC & DC conductivities as well as additional relaxation processes play a role

(in addition to the contribution of water)

In the frequency range between 100 MHz & 40 GHz the absorption of electromagnetic radiation as a function of frequency, temperature & ion concentration can be described by a universal set of parameters

Sub-cellular RF-filed Distribution & Absorption Depend on the Dielectric Properties of Biological Membranes

J. Gimsa

University of Rostock
Rostock, Germany

Sub-cellular distribution of RF-fields
inside the membranes and also inside the cells
were investigated using human red blood cells as a model
(they are homogeneous, abundant in blood and are well investigated)

Molecular properties strongly influence
the absorption of RF-fields in various cell compartments

Hidden "anisotropy dispersions" may result in
erroneous interpretation of the RF-filed distributions data

Membrane anisotropy may induce
higher local currents leading to higher energy dissipation

Averaging the absorption over the membrane layers
may lead to higher energy dissipation (up to 10-times) than
averaging over membrane properties

In layered membrane models
the absorption in the outer-most layer is dominating

PANEL DISCUSSION

The experimental & mathematical approaches used are appropriate to investigate the interaction of EMF with living matter

Do the measurements & calculations suggest any new, still unknown, interaction mechanism between EMF & tissues or cells

What are the physiological and health consequences of the interactions discussed

Are there suggestions for further research or new hypothesis concerning action mechanism of EMF, which could be tested

WORKSHOP CONCLUSIONS

The investigations are elegant & conducted well

The presentations are excellent

Studies on sensory systems gave new insights

All data raised more questions which need answers

Good science always raises more questions than answers
We may close some doors but we should not throw away the key
More doors may need to be opened to get into the big room

The current exposure guidelines are adequate for the purpose for which they were developed

The debate on long-term effects may not be resolved from the data presented in this workshop

It has to come in the context of human epidemiological studies

WORKSHOP CONCLUSIONS

Standardization & verification of exposure systems is extremely important for good research in RFR-exposure effects

It is not possible to convince people who believe that mobile phones are detrimental to human health

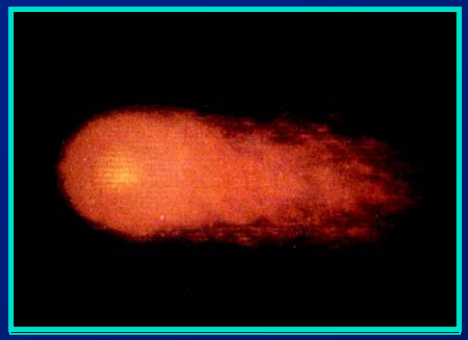
Genetic Damage Investigations

Most genotoxic agents are CARCINOGENS

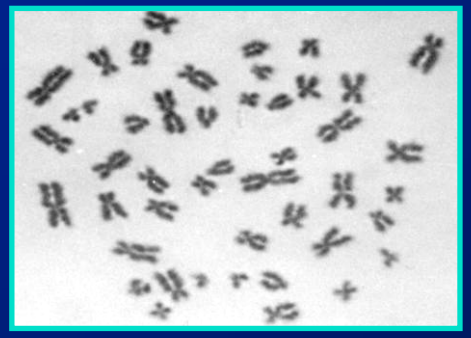
Non-genotoxic agents
which do NOT cause damage by themselves
can also contribute to carcinogenesis
by enhancing the damage induced by
known genotoxic agents
(Epigenetic Effect)

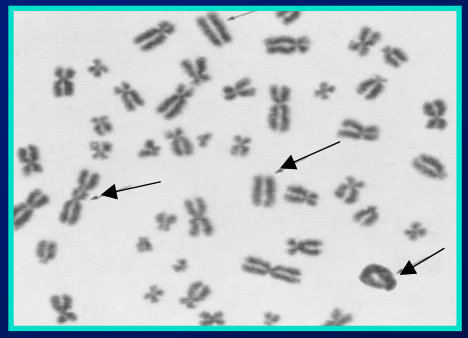
GENOTOXICITY

DNA Strand Breaks
SSB / DSB

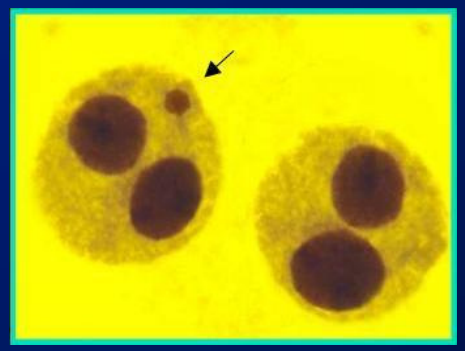


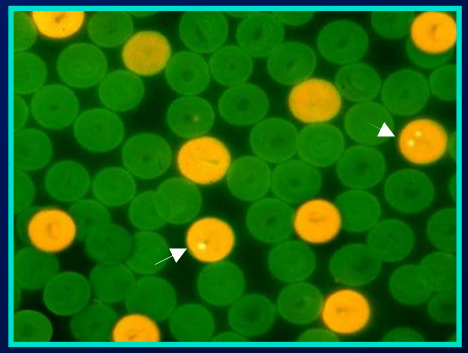
Chromosomal Aberrations
CA



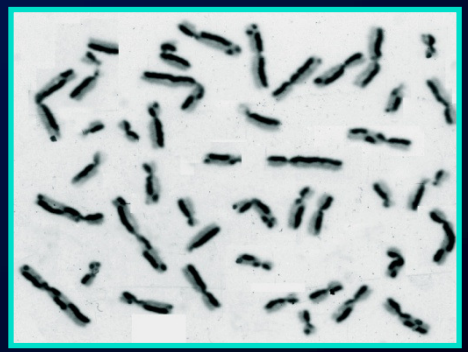


Micronuclei
MN





Sister Chromatid Exchanges
SCE



Radiation Research., 162, 481– 496, 2004

Controversial Cytogenetic Observations in Mammalian Somatic Cells Exposed to Radiofrequency Radiation

Vijayalaxmi & Guenter Obe

1990- 2003

" Qualitative Assessment "

Test System	Number of Studies Indicating Damage			Total
	Increase	No Increase	Inconclusive	
DNA Strand Breaks				
Whole-Body Exposure: Animals	4	1	0	5
In Vitro: Cultured Rodent Cells	0	3	0	3
In Vitro: Cultured Human Cells	0	2	1	3
In Vitro: Human Blood Lymphocytes	0	4	2	6
CA, MN & SCEs				
Whole-Body Exposure: Normal Animals	0	2	1	3
Whole-Body Exposure: Transgenic Animals	1	0	1	2
Whole-Body Exposure: Human	2	1	1	4
In Vitro: Cultured Rodent Cells	2	1	0	3
In Vitro: Human Blood Lymphocytes	3	11	4	18
In Vitro: RF alone (+/- Genotoxic Agents)	0	6	0	6
Total	12	31	10	53
	23%	58%	19%	
In Vitro: RFR +/- Genotoxic Agents	1	3	2	6
	17%	50%	33%	

Vijayalaxmi & Obe., Radiation Research. 162, 481 – 496, 2004

Recommendation

International Collaborative study
Co-ordinated in 6 separate centers
Adequate statistical power

Guide-lines

RFR exposures in a single laboratory
SAR 1 – 5 W/kg
Validated dosimetry
Adequate temperature controls
Multiple genotoxicity end-points
Multiple cell types of human origin
Different genetic backgrounds

Vijayalaxmi & Obe., Radiation Research. 162, 481 – 496, 2004

Meta-Analysis

Utilizes several QUANTITATIVE statistical methods for large data review & analysis

Widely used in biomedical research ESPECIALLY when the outcomes in different investigations are controversial

If considered separately, any one study may be too small to arrive at a generalized / unequivocal conclusion

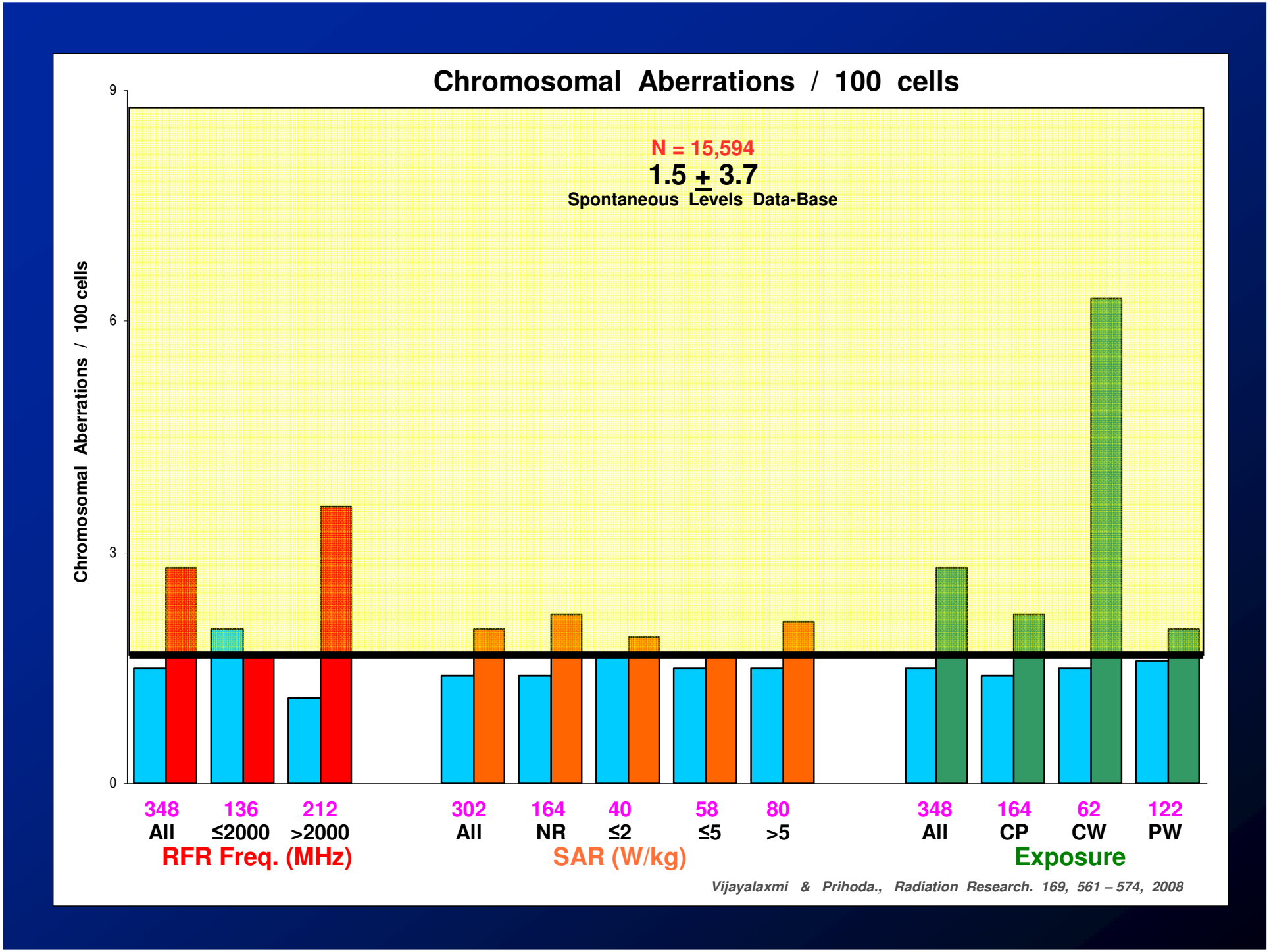
ANALYSIS OF THE COMBINED DATA FROM ALL RELATED STUDIES

an attractive alternative to strengthen the evidence from any individual study

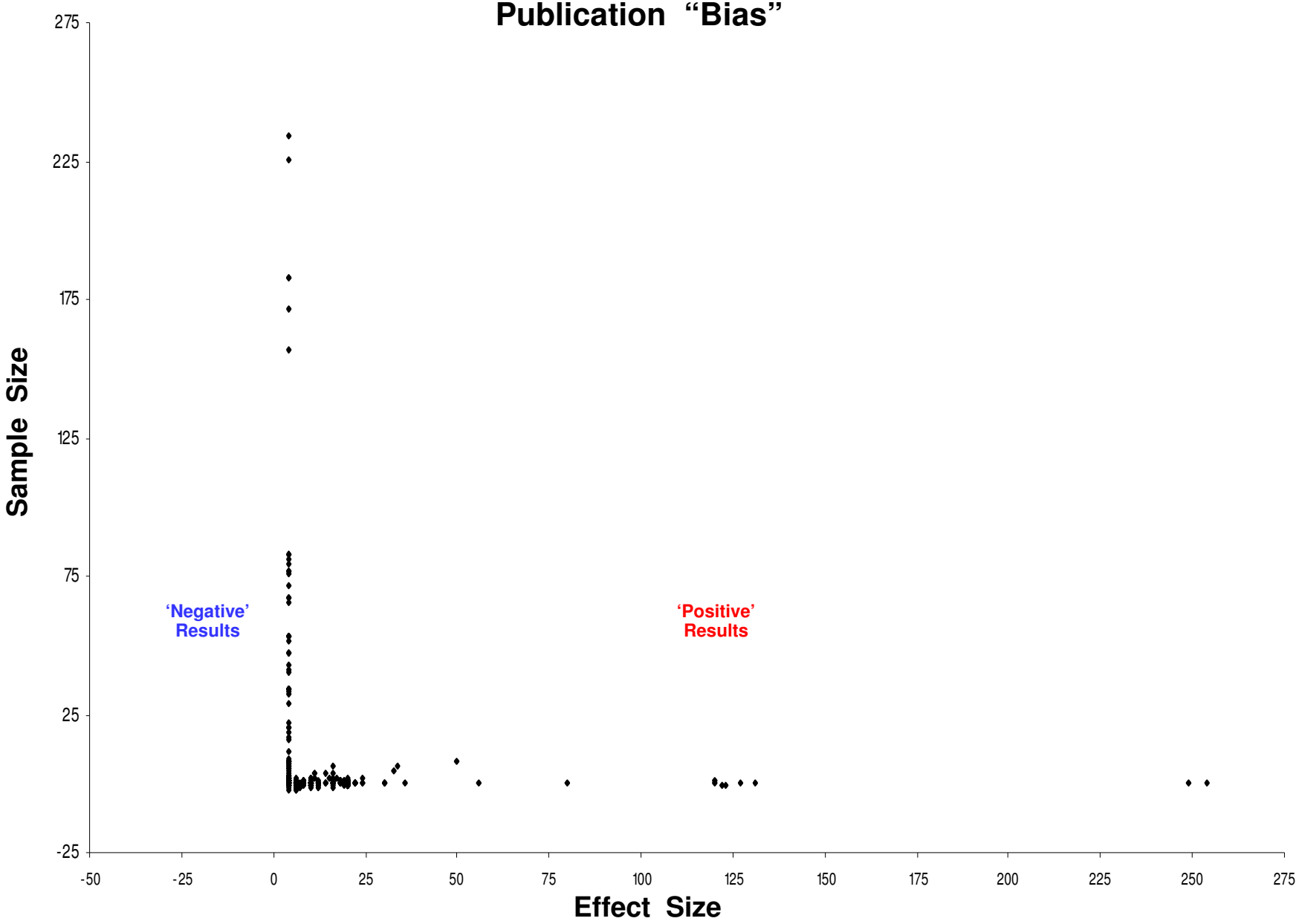
1990 - 2005 Publications

Sr#	First Author	Sr#	First Author	Sr#	First Author
1	Garaj-Vrhovac, 1990a	22	Vijayalaxmi, 1997a	43	Trosic, 2002
2	Garaj-Vrhovac, 1990b	23	Vijayalaxmi, 1997b	44	Gadhia, 2003
3	Kerbacher, 1990	24	Malyapa, 1998	45	Koyama, 2003
4	Ciaravino, 1991	25	Phillips, 1998	46	McNamee, 2003
5	Garaj-Vrhovac, 1991	26	Garaj-Vrhovac, 1999	47	Mashevich, 2003
6	Garson, 1991	27	Maes, 2000	48	Vijayalaxmi, 2003a
7	Fucic, 1992	28	Vijayalaxmi, 2000	49	Vijayalaxmi, 2003b
8	Garaj-Vrhovac, 1992	29	Zotti-Martelli, 2000	50	Zeni, 2003
9	Garaj-Vrhovac, 1993	30	Lalic, 2001	51	Hook, 2004
10	Maes, 1993	31	Li, 2001	52	Koyama, 2004
11	Sarkar, 1994	32	Maes, 2001	53	Lagroye, 2004a
12	d'Ambrosio, 1995	33	Sykes, 2001	54	Lagroye, 2004b
13	Lai, 1995	34	Vijayalaxmi, 2001a	55	Trosic, 2004
14	Maes, 1995	35	Vijayalaxmi, 2001b	56	Baohong, 2005
15	Lai, 1996	36	Vijayalaxmi, 2001c	57	Diem, 2005
16	Maes, 1996	37	d'Ambrosio, 2002	58	Gandhi, 2005a
17	Antonopoulos, 1997	38	Bisht, 2002	59	Gandhi, 2005b
18	Lai, 1997	39	McNamee, 2002a	60	Gorlitz, 2005
19	Maes, 1997	40	McNamee, 2002b	61	Komatsubara, 2005
20	Malyapa, 1997a	41	Mei-Bian, 2002	62	Zeni, 2005
21	Malyapa, 1997b	42	Tice, 2002	63	Zotti-Martelli, 2005

Vijayalaxmi & Prihoda., Radiation Research. 169, 561 – 574, 2008


Chromosomal Aberrations / 100 cells
N = 15,594
1.5 ± 3.7
Spontaneous Levels Data-Base
Chromosomal Aberrations / 100 cells
9
6
3
0
348
All
136
≤2000
212
>2000
RFR Freq. (MHz)
302
All
164
NR
40
≤2
58
≤5
80
>5
SAR (W/kg)
348
All
164
CP
62
CW
122
PW
Exposure
Vijayalaxmi & Prihoda., Radiation Research. 169, 561 – 574, 2008

Publication "Bias"



Vijayalaxmi & Prihoda., Radiation Research. 169, 561 – 574, 2008

Conclusions - Meta-Analysis

Difference between RFR-exposed and sham-/unexposed cells as well as the 'effect size' due to RFR exposure was small

At certain RFR exposure conditions there was a statistically significant increase in some genotoxicity end-points

The mean indices for CA, MN and SCE in RFR-exposed and sham-/unexposed cells were within the spontaneous levels reported in historical data-base

Considerable evidence for publication bias

Vijayalaxmi & Prihoda., Radiation Research. 169, 561 – 574, 2008