Utility of the NTP Data on Cell Phone RF Radiation for Assessing Human Health Risks

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NTP Study on Cell Phone RF Radiation: Objectives

1) **Test (challenge) the null hypothesis - cell phone RF radiation at non-thermal exposure intensities is incapable of inducing adverse health effects**

2) **Provide dose-response data that can be used to assess potential human health risks for any detected adverse effects**

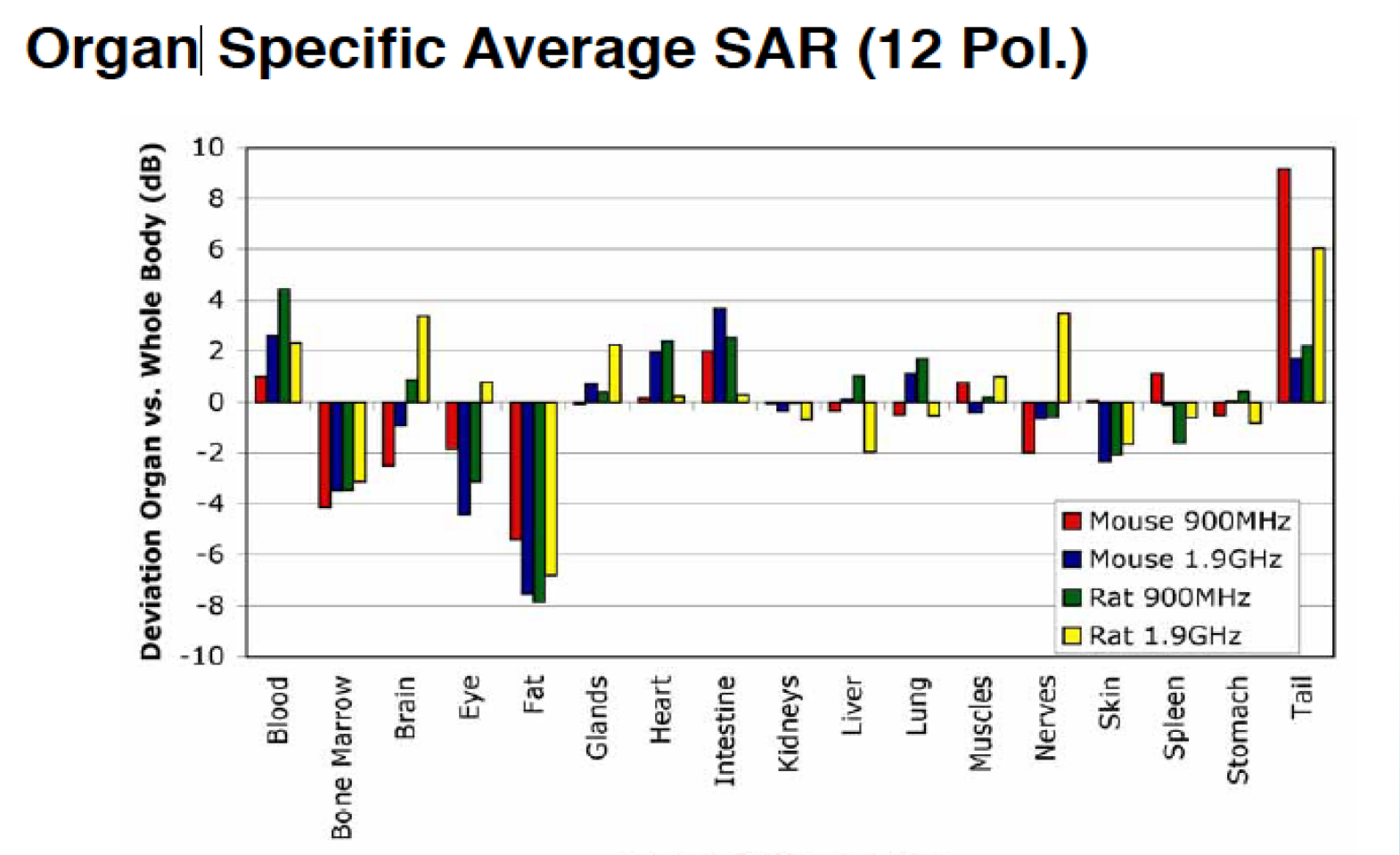
NTP Study on Cell Phone RF Radiation: Some Design Issues

1) **Highest exposure is limited by potential heating effects; thermal pilot study was conducted to not use exposures in which animals could not thermoregulate (body temperature increase < 1^{o}C).**

2) **FCC (1997) exposure limits for general population are 0.08 W/kg SAR averaged over the whole body and spatial SARs not to exceed 1.6 W/kg averaged over any 1 gram of tissue, and 8 W/kg average over any 1 gram of tissue (0.4 W/kg whole body) for occupational exposures.**

3) **Therefore to challenge the null hypothesis, daily exposures were extended to 9 hours, and animals could not be restrained.**

Organ SAR vs Whole Body SAR in Rats and Mice exposed in Reverberation Chambers



Based on high relative absorption in tail of rats at 1900 MHz and mice at 900 MHz, frequencies selected for NTP studies were 900 MHz for rats and 1900 MHz for mice

Null Hypothesis Disproven: Many Adverse Effects Identified

- Perinatal effects: dose-related reduction in pup birth weights (GSM and CDMA) and in weight gain of pups and dams during lactation
- Heart
  - Proliferative lesions: malignant schwannoma and Schwann cell hyperplasia in male rats (GSM and CDMA)
  - Right ventricular cardiomyopathy in male and female rats (GSM and CDMA); occurred early, dose-related, and increased severity with increasing exposure intensity
- Increased incidences and trends of DNA damage in brains of rats and mice (GSM and CDMA)
- Many equivocal conclusions; BUT proliferative responses (neoplasms and preneoplastic lesions) with GSM and CDMA indicate specific target organ effects, e.g., brain and prostate

Proliferative Lesions (neoplasms and hyperplasias) in the Brain of Male Rats

Male Rats	Sham	GSM (SAR mW/g)			CDMA (SAR mW/g)		
	0	1.5	3.0	6.0	1.5	3.0	6.0
Lesion	Incidence, %						
Glioma[a]	0	3.3	3.3	2.2	0	0	3.3
Glial cell hyperplasia	0	2.2	3.3[b]	1.1[b]	2.2	0	2.2[b]
Total proliferative	0	5.5*	6.6*	3.3	2.2	0	5.5*

* $p<0.05$

[a] Historical control rate (all routes) = 2/190 (1.1%, range 0-4%)

[b] Marked severity of glial cell hyperplasia for one rat in these dose groups; “the hyperplastic lesions are within a continuum leading to malignant glioma”

Same Data for Brain, Different Conclusions

- **NTP (2016): the hyperplastic lesions and neoplasms of the heart and brain observed in male rats are considered *likely the result of whole-body exposures* to GSM- or CDMA-modulated RFR**
- **NTP (2018): there was some evidence of carcinogenic activity of GSM-modulated and of CDMA-modulated cell phone RFR at 900 MHz in male Sprague Dawley rats based on schwannomas in the heart; the incidences of *malignant glioma in the brain may have been related* [i.e., equivocal] to GSM- or to CDMA- modulated cell phone RFR (900 MHz)**

Proliferative Lesions (neoplasms and epithelial hyperplasias) in the Prostate Gland of Male Rats

Male Rats	Sham	GSM (SAR mW/g)			CDMA (SAR mW/g)		
	0	1.5	3.0	6.0	1.5	3.0	6.0
Lesion	**Incidence, %**						
Adenoma/carcinoma[a]	2.2	2.2	7.8[b]	3.3	0	2.2	1.1
Epithelial hyperplasia[c] (severity)	5.5 (1.2)	14.4 (1.6)	12.2 (1.9)	12.2 (2.4)	12.2 (1.6)	10.0 (1.7)	17.6* (2.2)
Total proliferative	7.7	16.6	20.0*	14.4[d]	12.2	12.2	18.7*

* $p<0.05$

[a] Historical control rate for adenomas (all routes) = 2/240 (0.8%, range 0-2%)

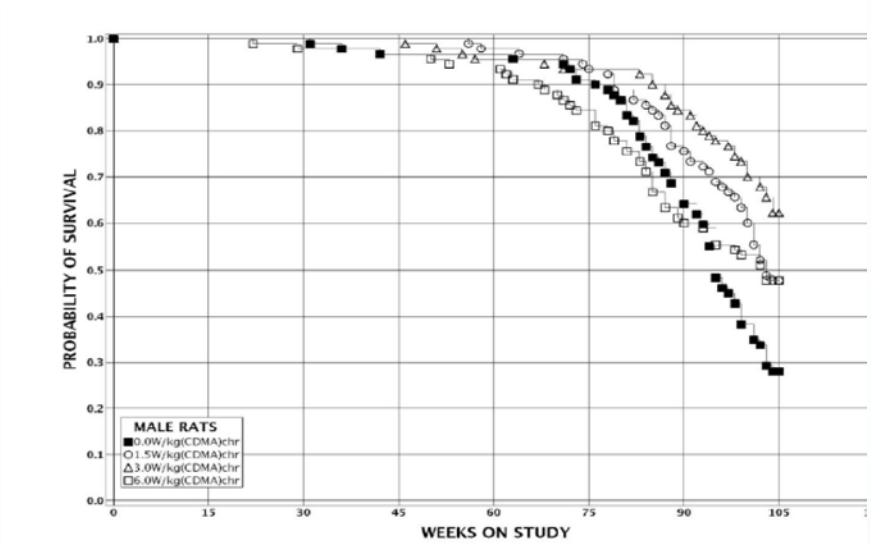
[b] Exceeded historical control range for all rat strains used by NTP

[c] Increased severity of these preneoplastic lesions with increasing SAR (GSM or CDMA)

[d] One animal diagnosed with adenoma and hyperplasia

What About Survival Differences Between Exposed and Sham Control Male Rats?

1)



No significant difference in mean survival between controls and 6 W/kg CDMA male rats (same survival at 93 weeks)

2) No glial cell hyperplasias (potential precancerous lesions) or heart schwannomas were observed in any control rat, even though glial cell hyperplasia was detected in exposed rats as early at week 58 of the 2-year study and heart schwannomas were detected as early as week 70 in exposed rats. Therefore, survival was sufficient to detect tumors or pre-cancerous lesions in the brain and heart of control rats

3) Unusually high CPN severity (3.7) in control male rats; mean severity in other NTP studies with Harlan SD rats = 2.9, range 2.5-3.2

There is *Some Evidence of Carcinogenic Activity* in Male Mice Exposed to GSM-modulated RFR

	Sham	GSM (SAR mW/g)		
	0	2.5	5	10
LUNG	Incidence, (%)			
Alveolar/Bronchiolar adenoma or carcinoma[a]	26 P=0.040	27	36	38 P=0.074
A/B carcinoma	14	13	18	20
SKIN				
Malignant fibrous histiocytoma[b]	1.1 P=0.093	0	5.6 P=0.124	3.3

[a] Historical control rate: 24 ± 5%, range 16-34%

[b] Historical control rate: 2/589 (0.3% ± 0.7%, range 0-2%)

Cancer Epidemiology

- **IARC (2013) classification of RF radiation as ”possibly carcinogenic to humans” is based largely on both the Interphone and Swedish case-control studies (Hardell et al.). For glioma and acoustic neuroma (vestibular schwannoma), “the Working group concluded that these findings [significant elevations in odds ratios] could not be dismissed as reflecting bias alone, and that a causal interpretation was possible.”**

- **“Elevated odds ratios observed at the highest level of cumulative call time could be due to chance, reporting bias or a causal effect” (Interphone, 2011)**

- **Adjustment for selection and recall biases in the Canadian data from the Interphone study did not affect the significant increase in the odds ratio for glioma (Momoli et al., 2017)**

NTP Study on Cell Phone RF Radiation: Utility for Assessing Potential Human Health Risks

- Identified target organs (tumors & preneoplastic lesions)
  - Rats: heart, brain (including DNA damage), prostate gland
  - Mice: skin, lungs
- Concordance between rats and humans in cell types affected (glial and Schwann cells) by RF radiation strengthens the animal-to-human association.
- Health risk estimates (by FDA) should be based on response rates (i.e., incidence of tumors and preneoplastic lesions) as a function of tissue dosimetry (absorbed power x hours per day of exposure) and duration of exposure in animals extrapolated to RF dosimetry in exposed humans
- Even a small increase in cancer risk could have a serious health impact due to the widespread use of cell phones: ~300 million in the US and 5 billion worldwide