資料2
（今井田構成員）

生体電磁環境に関する研究戦略会議

領域：「高周波」

分野：「動物」

これまでのこの分野での研究状況

問題点

動物を用いた発がん性リスクに関するこの分野のこれまでの日本での研究状況

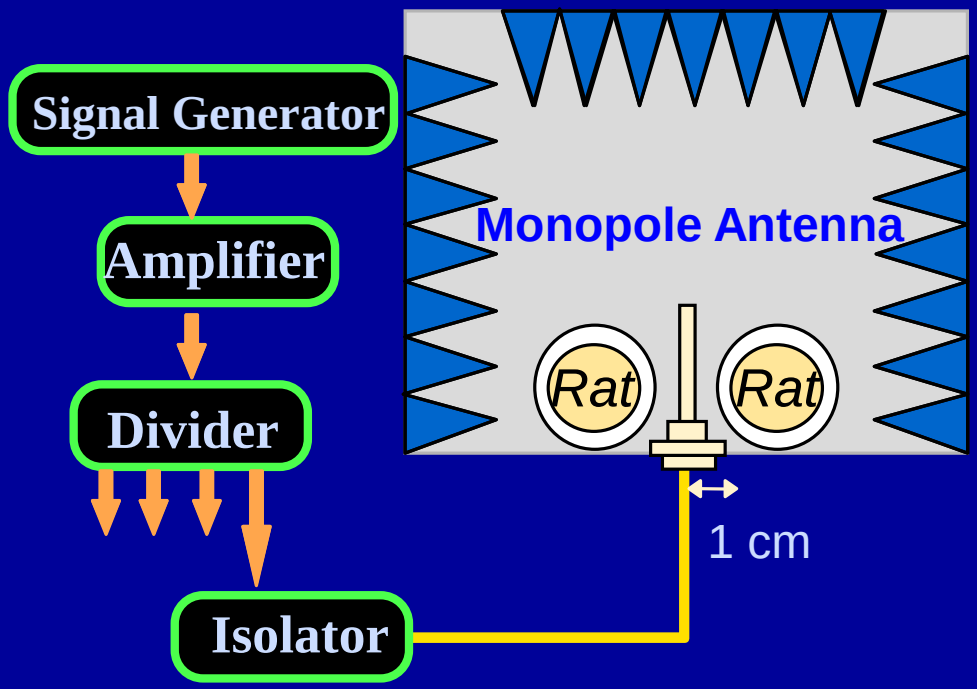
1) Liver carcinogenesis（肝発癌に関して）

2) Skin carcinogenesis（皮膚発がんに関して）

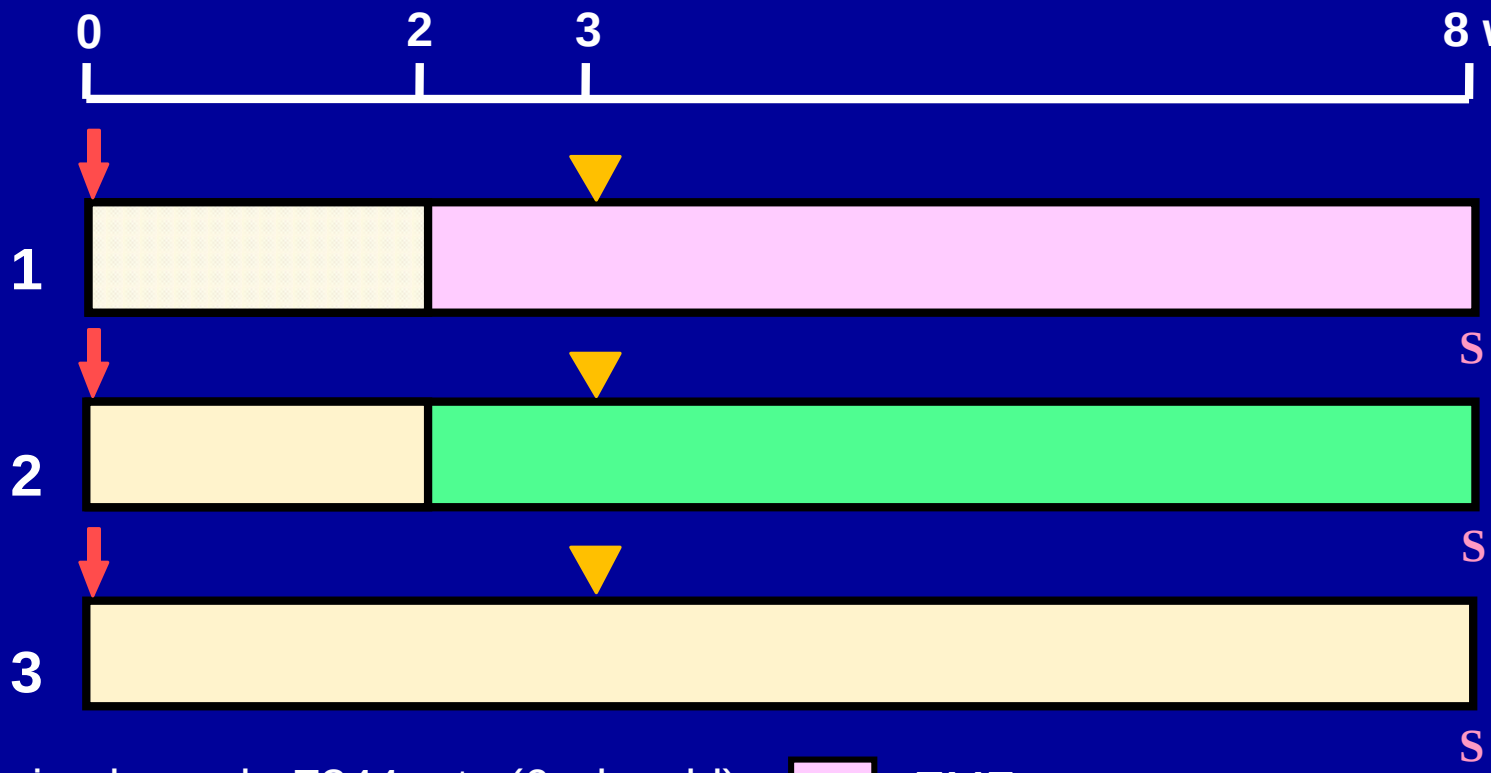
3) Brain carcinogenesis（脳腫瘍発がんに関して）

Effects of the Electromagnetic Field (900 MHz and 1.5 GHz) on Rat Liver Carcinogenesis

A medium term liver bioassay system



	Experiment I	Experiment II
Frequency	929 MHz	1,439 MHz
Antenna input	0.52 W	0.33 W
SAR (liver)	2.0 W/kg	2.0 W/kg
Exposure	1.5 hrs/day, 5 days /week. 6 weeks	
Modulation	Time division multiple access	



Animal : male F344 rats (6 wks old)

: EMF

Experiment Ⅰ : 929 MHz

Experiment II : 1,439 MHz (1.5GHz)

:DEN(diethylnitrosamine), 200 mg/kg, ip injection

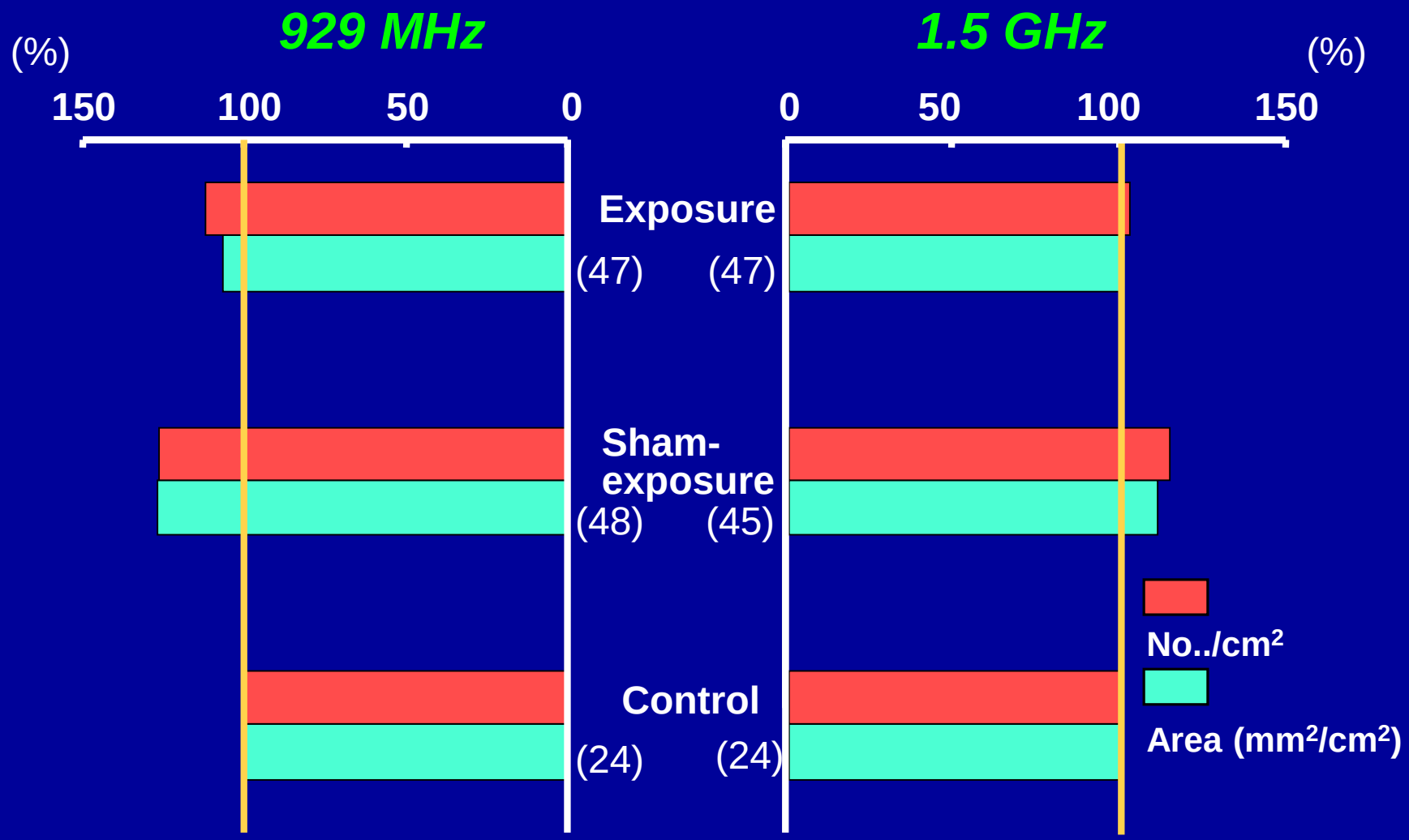
: 2/3 partial hepatectomy

: sham exposure

S : Sacrifice, glutathione S-transferase placental form immunohistochemistry

ACTH, Corticosterone, Melatonin

Experimental Design



Numbers in parenthesis indicate effective number of rats

Quantitative Data of GST-P Positive Foci in the Liver

Effects of the Electromagnetic Field (900 MHz and 1.5 GHz) on Rat *Liver* Carcinogenesis

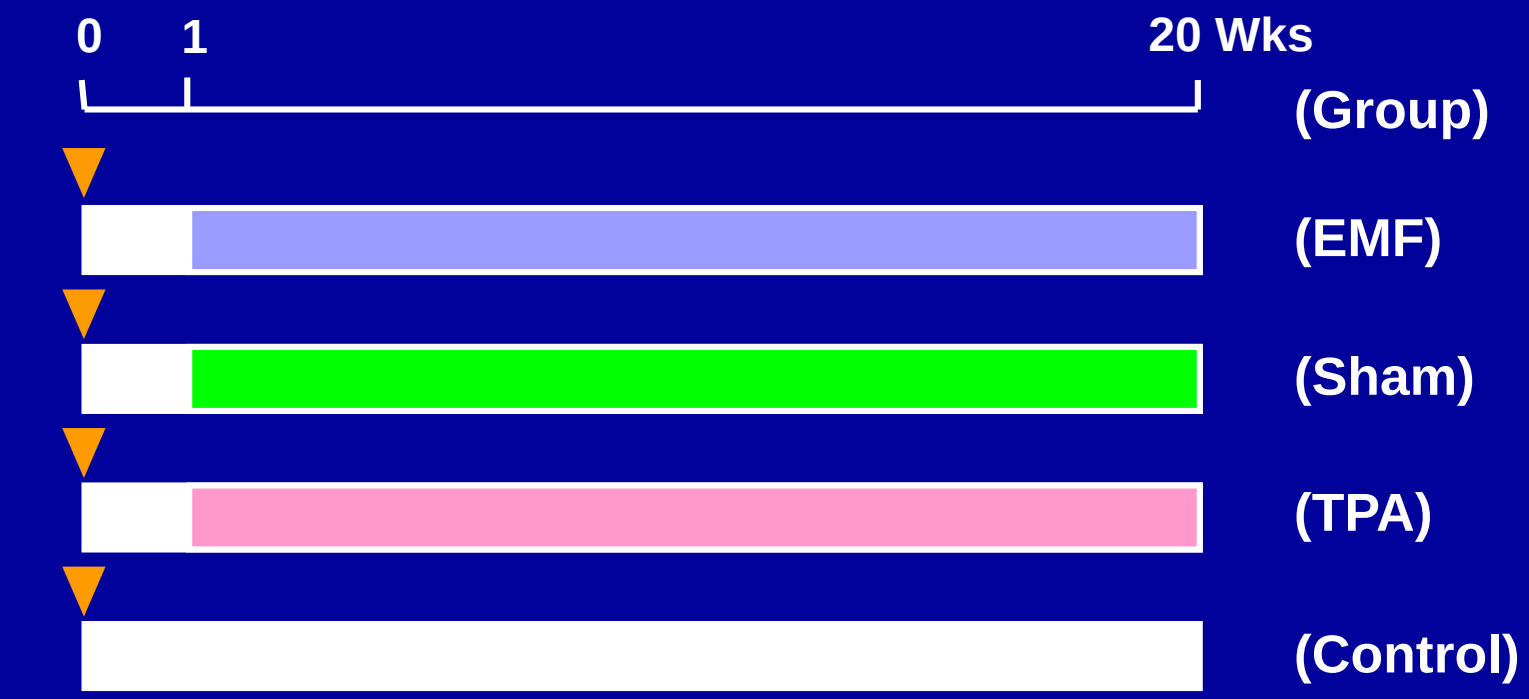
Imaida K, Taki M, Yamaguchi T, Ito T, Watanabe S, Wake K, Aimoto A, Kamimura Y, Ito N, Shirai T.
***Lack* of promoting effects of the electromagnetic near-field used for cellular phones (929.2 MHz) on rat liver carcinogenesis in a medium-term liver bioassay.**
Carcinogenesis 19:311-314 1998

Imaida,K., Taki,M., Watanabe, S., Kamimura, Y., Ito, T., Yamaguchi, T., Ito, N. and Shirai, T.
The 1.5 GHz electromagnetic near-field used for cellular phones *does not promote* rat liver carcinogenesis in a medium-term liver bioassay. *Jpn J. Cancer Res.*, 89: 995-1002, 1998

Effects of EMF on Mouse Skin Carcinogenesis

DMBA*-skin two step carcinogenesis model

***7,12-dimethylbenz[a]anthracene**



Animal : CD-1 female mouse

: 7,12-dimethylbanz(a)anthracene(DMBA)100 μg/mouse

: Exposure of electromagnetic near fields (5 days/week, 19 weeks)

: Sham exposure

: 12-*O*-tetradecanoylphorobol-13-acetate(TPA); 4.0 μg/mouse, as a positive control

Effects of 1.5 GHz EMF on DMBA-induced mouse skin carcinogenesis

Incidences of skin tumors

Group	No. of rats	Incidence (%)		
		Papilloma	Carcinoma	Total
EMF	48	0 (0)	0 (0)	0 (0)
Sham	48	0 (0)	0 (0)	0 (0)
TPA	30	29 (96.6)***	2 (6.7)	29 (96.6)***
Control	30	1 (3.3)	0 (0)	1 (3.3)

***, P < 0.001 vs Control

Effects of EMF on Mouse Skin Carcinogenesis

DMBA-skin two step carcinogenesis model

Imaida, K., Kuzutani, K., Wang, J., Fujiwara, O., Ogiso, T., Kato ,K., and Shirai, T.

***Lack of promotion* of 7,12-dimethylbenz[a]anthracene-initiated mouse skin carcinogenesis by 1.5 GHz electromagnetic near fields**.

***Carcinogenesis*,** 22: 1837-1841, 2001

Effects of EMF on Brain and Spinal Cord Carcinogenesis

ENU*-induced central nervous system carcinogenesis model

*** ENU: Ethylnitrosourea**

Experimental Design

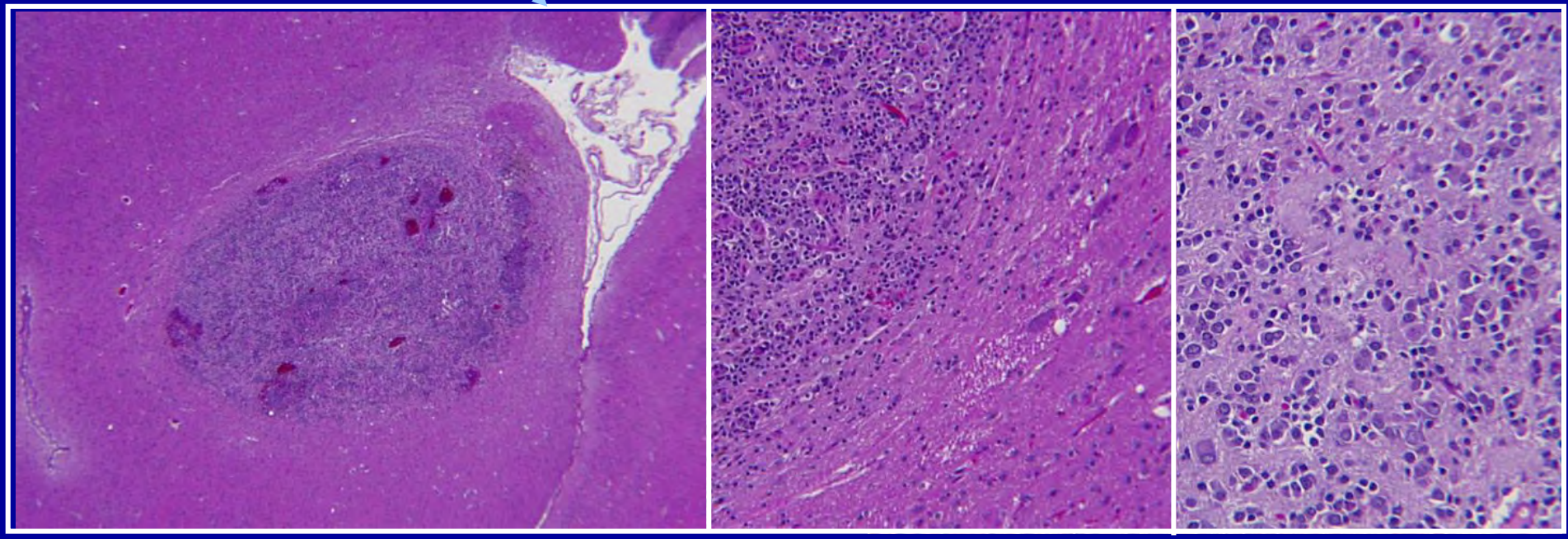
1. 103 pregnant F344 rats with a certification of mating date were purchased from Charles River Japan.
2. A single iv injection of N-ethyl-N-nitrosourea (ENU) at a dose of 4 mg/kg body weight on the gestational day 18 (tail vein).
3. 200 F1 rats for each sex from 285 F1 females and 266 F1 males were used for experiment.
4. 50 F1 rats for each sex from control mothers were served as control.

Group	ENU	EMF	Levels of EMF (SAR:W/Kg)	No. of animals	
				Female	Male
1	**–**	**–**	**0**	**50**	**50**
2	**+**	**–**	**0**	**50**	**50**
3	**+**	**– (sham)**	**0**	**50**	**50**
4	**+**	**+ (low)**	**0.67**	**50**	**50**
5	**+**	**+ (high)**	**2.0**	**50**	**50**

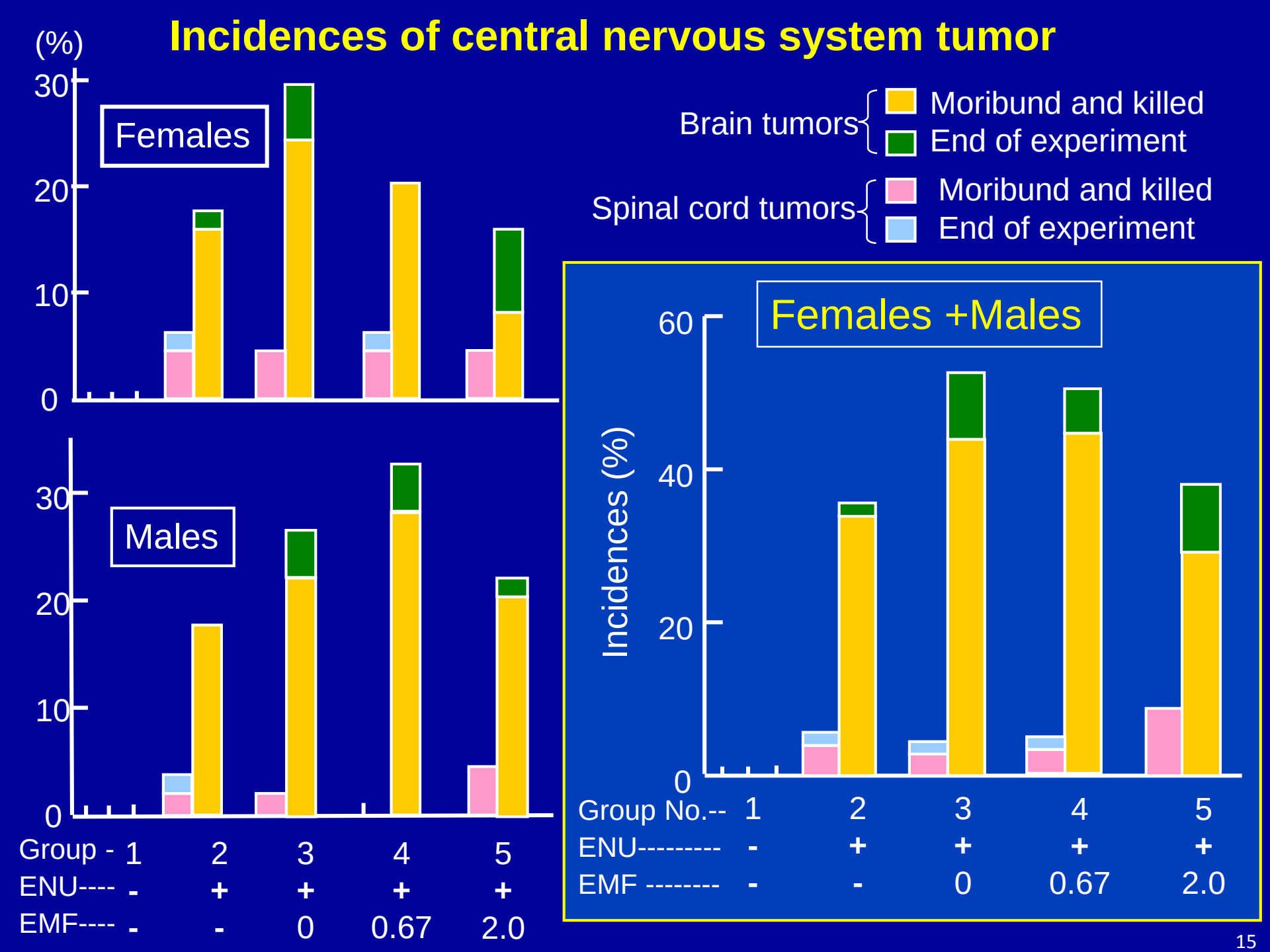
Pups: after randomization, 3 per cage

63 rats for each sex were prepared as Dummy animals and 9 animals for Monitoring.

Astrocytoma



Incidences of central nervous system tumor



Effects of EMF on Brain and Spinal Cord Carcinogenesis

ENU-induced central nervous system carcinogenesis model

Shirai T, Kawabe M, Ichihara T, Fujiwara O, Taki M, Watanabe S, Wake K, Yamanaka Y, Imaida K and Tamano S

Chronic Exposure to A 1,439 GHz Electromagnetic Near-field Used for Cellular Phones *Does Not Promote* Ethylnitrosourea-induced Central Nervous System Tumors in F344 Rats.

Bioelectromagnetics, 26:59-68, 2005

The Ministry of Public Management, Home Affairs, Posts and Telecommunications, Japan

Report of Partial Findings from the National Toxicology Program Carcinogenesis Studies of Cell Phone Radiofrequency Radiation in Hsd: Sprague Dawley® SD rats (Whole Body Exposures)

Draft 5-19-2016

Table of Contents

Cell phone RFR research program

- Three-phase toxicology and carcinogenicity studies in Harlan Sprague Dawley rats and B6C3F$_1$ mice
  - **5-day pilot** studies at SARs of 4-12 W/kg in young and aged rats and mice and pregnant rats (10 studies)
  - **28-day prechronic** toxicology studies
  - **2-year** toxicology and carcinogenicity studies
- Daily exposure to RFR in reverberation chambers for ~9 hours (18 hr 20 min per day in 10 min on/10 min off cycles)
  - Rats exposed to either GSM- or CDMA-modulated signals at 900 MHz beginning *in utero*
  - Mice exposed to GSM- and CDMA-modulated signals at 1900 MHz beginning at 5 weeks of age

Chronic toxicology/carcinogenicity study design – Rats

- Time-mated, pregnant, female Harlan Sprague Dawley rats (n=56 per group) randomly assigned to SAR groups of 0, 1.5, 3, and 6 W/kg GSM or CDMA RFR
  - ~9 hrs exposure/day (10 min on/off cycling), 7 days/week
  - Exposures initiated *in utero* on GD 5
  - Exposure continued throughout gestation and lactation
  - Dams removed at weaning on PND 21; pups housed individually on PND 35
- On PND 21, weanlings randomly selected for chronic exposure
- Interim evaluation after 13 weeks (n=15/sex/exposure group)
- Study termination after 107 weeks (n=90/sex/exposure group)

Pathology findings – Brain

Hyperplastic Brain Lesions in Male Rats

	Control		GSM Modulation			CDMA Modulation		
	0 W/kg		1.5 W/kg	3.0 W/kg	6.0 W/kg	1.5 W/kg	3.0 W/kg	6.0 W/kg
Number examined	90		90	90	90	90	90	90
Malignant glioma‡	0*		3 (3.3%)	3 (3.3%)	2 (2.2%)	0	0	3 (3.3%)
Glial cell hyperplasia	0		2 (2.2%)	3 (3.3%)	1 (1.1%)	2 (2.2%)	0	2 (2.2%)

‡ Historical control incidence in NTP studies: 11/550 (2.0%), range 0-8%

* Significant SAR-dependent trend for CDMA exposures by poly-6 ($p < 0.05$)

動物を用いた発がん性リスクに関するこの分野のこれまでの日本での研究状況

1) **Liver** carcinogenesis（肝発癌に関して）

2) **Skin** carcinogenesis（皮膚発がんに関して）

3) **Brain** carcinogenesis（脳腫瘍発がんに関して）

上記のいずれの臓器発がんに関して、EMFによる発がん促進作用は認めなかった。

NTP study の結果に関しては、国際的な協調を踏まえた検討が必要