National Institute "B. Ramazzini"

Cesare Maltoni Cancer Research Center

Syncarcinogenic effects of the exposure to low dose of γ radiation and to 50 Hz MF on mammary gland of female rats

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INTERACTION OF WEAK ELECTROMAGNETIC FIELDS WITH LIVING MATTER
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The integrated experimental project of the Ramazzini Institute on ionizing and non ionizing radiations

The experimental project of the RI on electromagnetic fields

- Mega-experiments on ionizing radiation
- Mega-experiments on non-ionizing radiation

  > ELFMF

  > RFEMF

- Number of rats involved in the experiments: 18.953

The integrated project on γ radiation: overall design

N. experiment	N. of animals M+F	Treatment			
		Type	Dose (rads)	Schedule	Duration
1	4016	Direct irradiation at 6-8 weeks of age	300;100; 10; 0	One off or fractionated	Life-span
2	2799	Irradiation of pregnant females at 12° day of pregnancy	100; 50; 10; 0	One off	Life-span
3	2557	Irradiation of male breeders before matching	300; 100; 10; 0	One off	Life-span
Total	9372				

The integrated project on 50 Hz MF: overall design

Experiments	No. of animals	treatment [a] μ-Tesla	Other treatment	Duration
Experiment 1 [b]	5029	1000; 100; 20; 2; 0	___	Life-span
Experiment 2	805	1000; 0	Formaldheyde, 50 ppm in drinking water from 6 weeks of age	Life-span
Experiment 3	657	1000; 20; 0	γ- radiation: 10 rads one shot at 6 weeks of age	Life-span
Experiment 4	642	1000; 0	Aflatoxin B1, 70 μg/rat 9 times between 6-7 weeks of age	Life-span
Total	**7133**			

[a] The treatment started from fetal life until spontaneous death

[b] The control group of over 500 M and 500 F is shared with experiments 2 and 3

The project on 1,8 GHz RFEMF: the experiment desi

Group number	Age at start	Number of animals (M+F)	Treatment (Volt/meter)	Duration
I	embryo	409	50 Volt/meter	Lifespan
II	embryo	411	25 Volt/meter	Lifespan
III	embryo	811	5 Volt/meter	Lifespan
IV	embryo	817	0 Volt/meter (control)	Lifespan
TOTAL		**2,448**		

First results of the integrated project

The syncarcinogenic effects of the exposure to low dose of γ radiation (one-shot) and to 50 Hz MF for the life-span on mammary gland

- Background
- Rationale
- Objective
- Endpoints

Experiment on 50 Hz MF and γ-radiation exposure

Background

- Incidence and mortality for breast cancer among women is still high in western countries
- Mammary gland tissue is very sensitive to the carcinogenic effects of radiation both in humans and in rats

Mammary cancers and their precursors in female S-D rats exposed to γ-radiations, one shot at 6 wks of age, and followed until spontaneous death

RESULTS

No. of animals/ dose (rad)	Cancers and their precursors (No. per 100 rats)		
	Dysplasias (D) [a]	Carcinomas (C)	D+C
205 (300)	11.7	52.7	64.4
301 (100)	19.9	35.5	55.5
522 (10)	28.5	18.4	47.0
537 (0)	7.4	16.0	23.4

[a] dysplasia in mammary gland plus dysplasia in fibroadenomas

Experiment on 50 Hz MF and γ-radiation exposure

Rationale

Given the exposure of women to low doses of ionizing radiation for diagnostic purposes and to the ubiquitous MF generated during the distribution and use of electricity, we believed it to be of public health interest to use the female S-D rat model to evaluate if the exposure to low dose γ-radiation and 50 Hz-MF experimentally increases the risk of mammary cancer.

Experiment on 50 Hz MF and γ-radiation exposure

Objective

To evaluate if the development of mammary tumors induced by the exposure to one shot of 10 rads of γ-radiation at 6 weeks of age could be altered by the exposure to 50 Hz-MF from fetal life until spontaneous death.

Experiment on 50 Hz MF and γ-radiation exposure

End points

- The cumulative prevalence of mammary lumps, clinically observed during biophase
- Tumor incidence and their precursors, histologically confirmed
- Total number of tumors and their precursors per 100 animals
- Cumulative prevalence of mammary carcinomas

Experiment on 50 Hz MF and γ-radiation exposure: experimental design

Group	Animals		Treatment		Duration of the exp.
	Sex	No.	μT [a]	Rad [b]	
I	F	112	1000	10	Life-span
II	F	107	20	10	Life-span
III	F	270	1000	-	Life-span
IV	F	105	-	10	Life-span
V	F	501	-	-	Life-span
Total		1095			

[a] : began at 12° day of fetal life until spontaneous death

[b] : administered one shot at 6 weeks of age

50-Hz magnetic fields exposure system

- The goal was to generate fields representative of power line systems
- A circular structure with 24 coils was mounted on an aluminum support structure. The design yields low external fields, which allowed the housing of multiple structures in a reasonable vicinity of one another.
- The magnetic field uniformity was as +/- 10%
- The magnetic field was controlled by monitoring the current
- A +/- 3% current range were mantained
- A magnetic field probe was used for monitoring the fields

50-Hz magnetic fields exposure system

50-Hz magnetic fields exposure system

Apparato espositivo ai raggi gamma

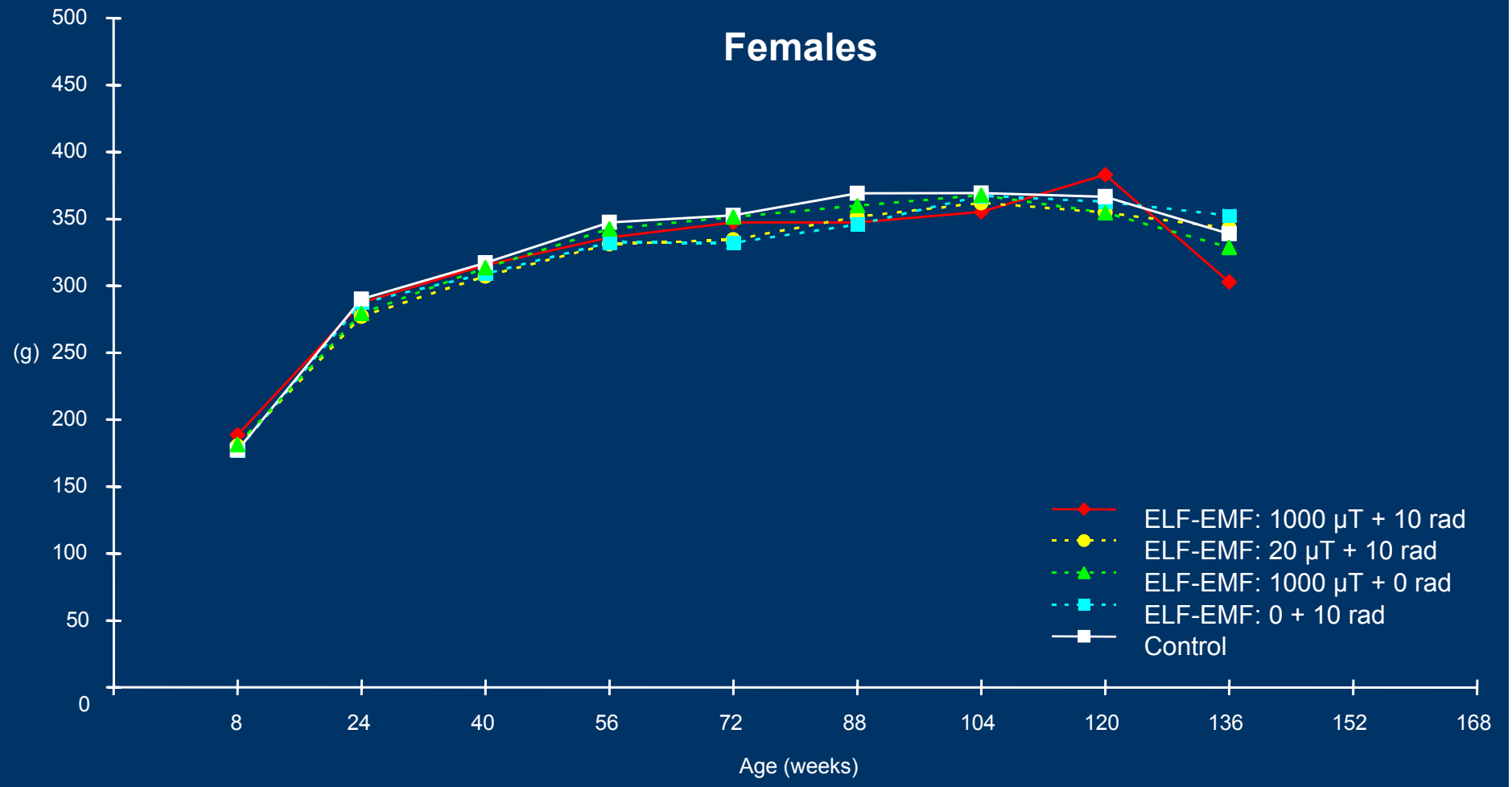
Experiment on 50Hz MF and γ radiation exposure: the conduct of the experiment

- Randomization
- Daily control
- Feed and water consumption
- Body weight evaluation
- Clinical mammary lung monitoring
- Complete necropsy at death

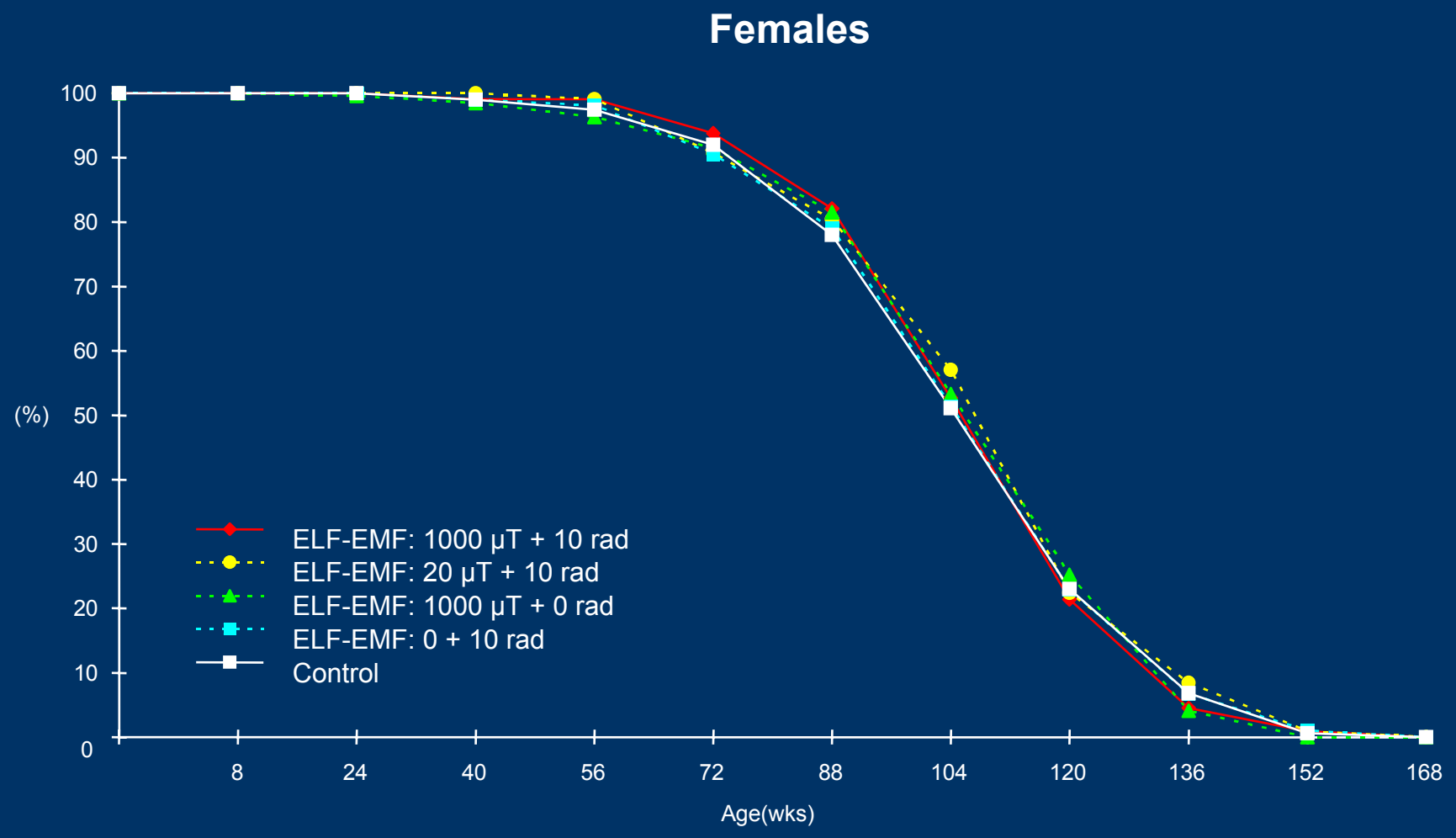
Experiment on 50Hz MF and γ radiation exposure

The results

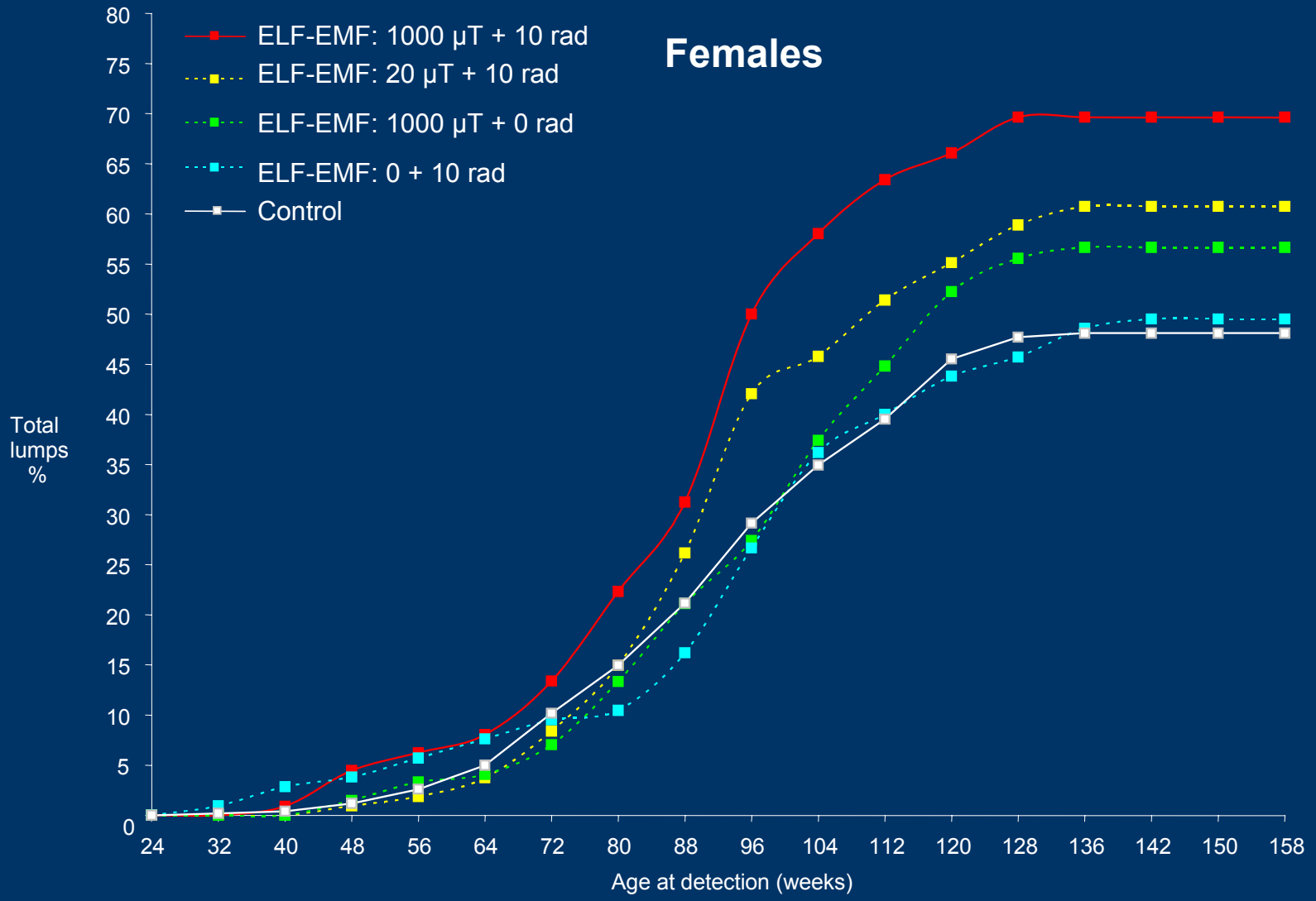
Experiment on 50 Hz MF and γ-radiation exposure: Body weight



Experiment on 50 Hz MF and γ-radiation exposure: Survival



Experiment on 50 Hz MF and γ-radiation exposure



Cumulative prevalence of glandular MAMMARY LUMPS clinically observed during biophase

Experiment on 50 Hz MF and γ-radiation exposure: fibroadenomas histopathologically evaluated

Females No.	Treatment		Fibroadenomas	
	μT	Rad	Bearing animals %	Total per 100 animals
112	1000	10	45.5	68.8
107	20	10	47.7	59.8
270	1000	-	43.7	60.7
105	-	10	41.0	52.4
501	-	-	41.3	53.5

Experiment on 50 Hz MF and γ-radiation exposure: precursors of mammary carcinomas

Females No.	Treatment		AIMG plus AFA	
	μT	Rad	Bearing animals %	Total per 100 animals
112	1000	10	**15.2****	20.5
107	20	10	**15.0****	16.8
270	1000	-	6.3	6.3
105	-	10	4.8	4.8
501	-	-	4.0	4.2

AIMG = Atypical iperplasia in mammary gland; AFA = Atypical fibroadenomas

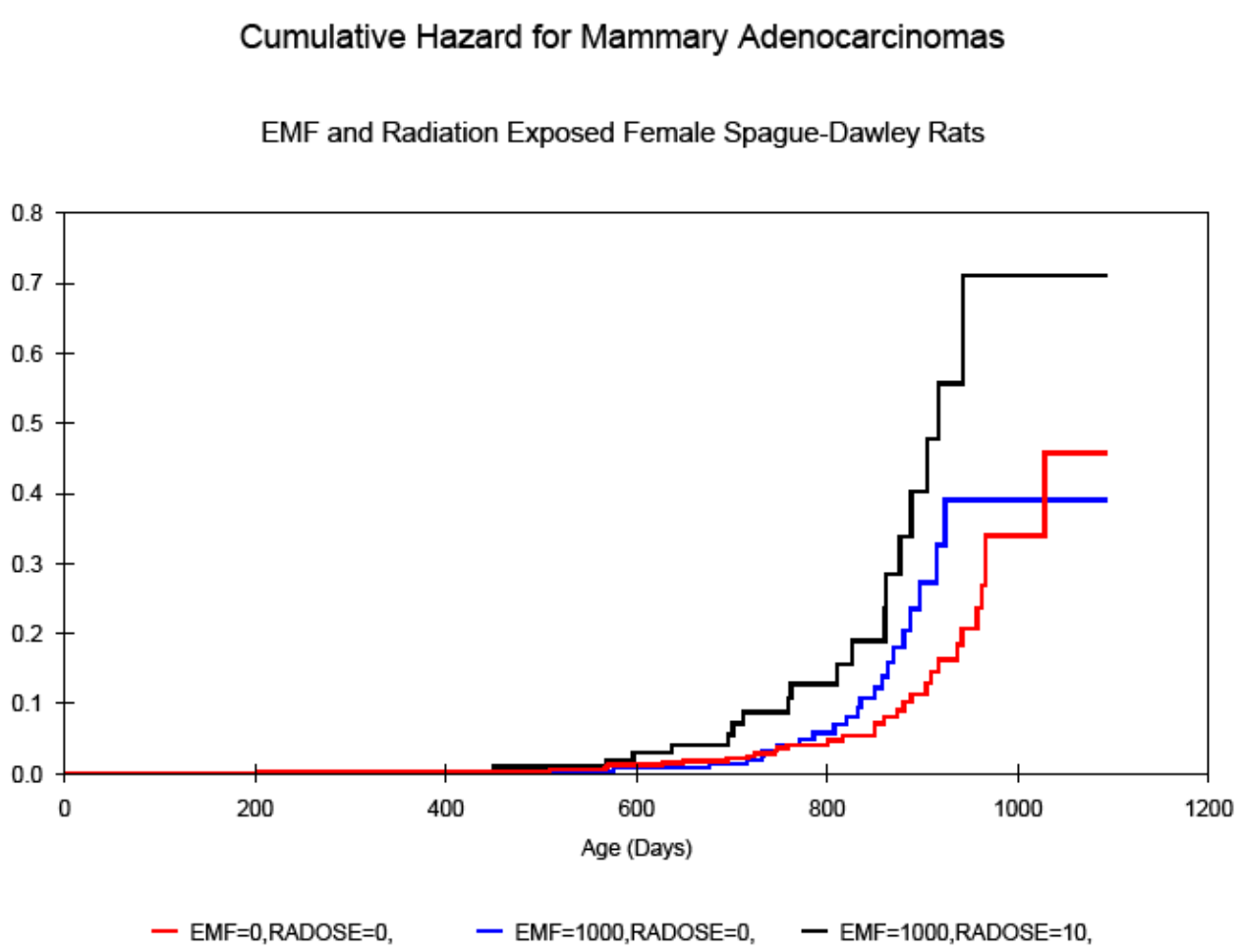
**significant ($p<0.01$) using Cox Regression Model

Experiment on 50 Hz MF and γ-radiation exposure: mammary carcinomas

Females No.	Treatment		Carcinomas	
	μT	Rad	Bearing animals %	Total per 100 animals
112	1000	10	**16.1****	**17.0**
107	20	10	7.5	8.4
270	1000	-	8.1	8.5
105	-	10	7.6	7.6
501	-	-	6.4	6.4

**significant ($p<0.01$) using Cox Regression Model

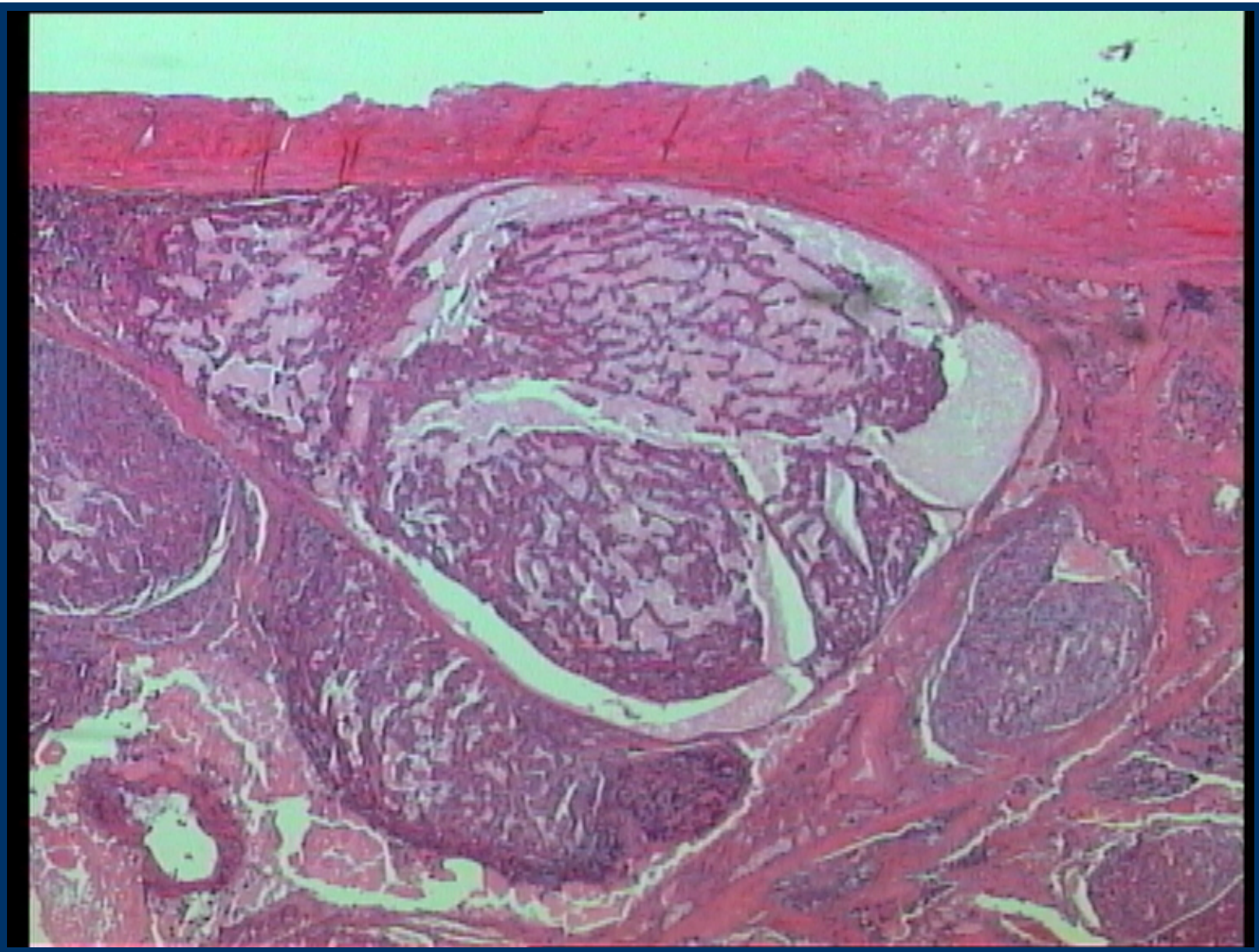
Experiment on 50 Hz MF and γ-radiation exposure



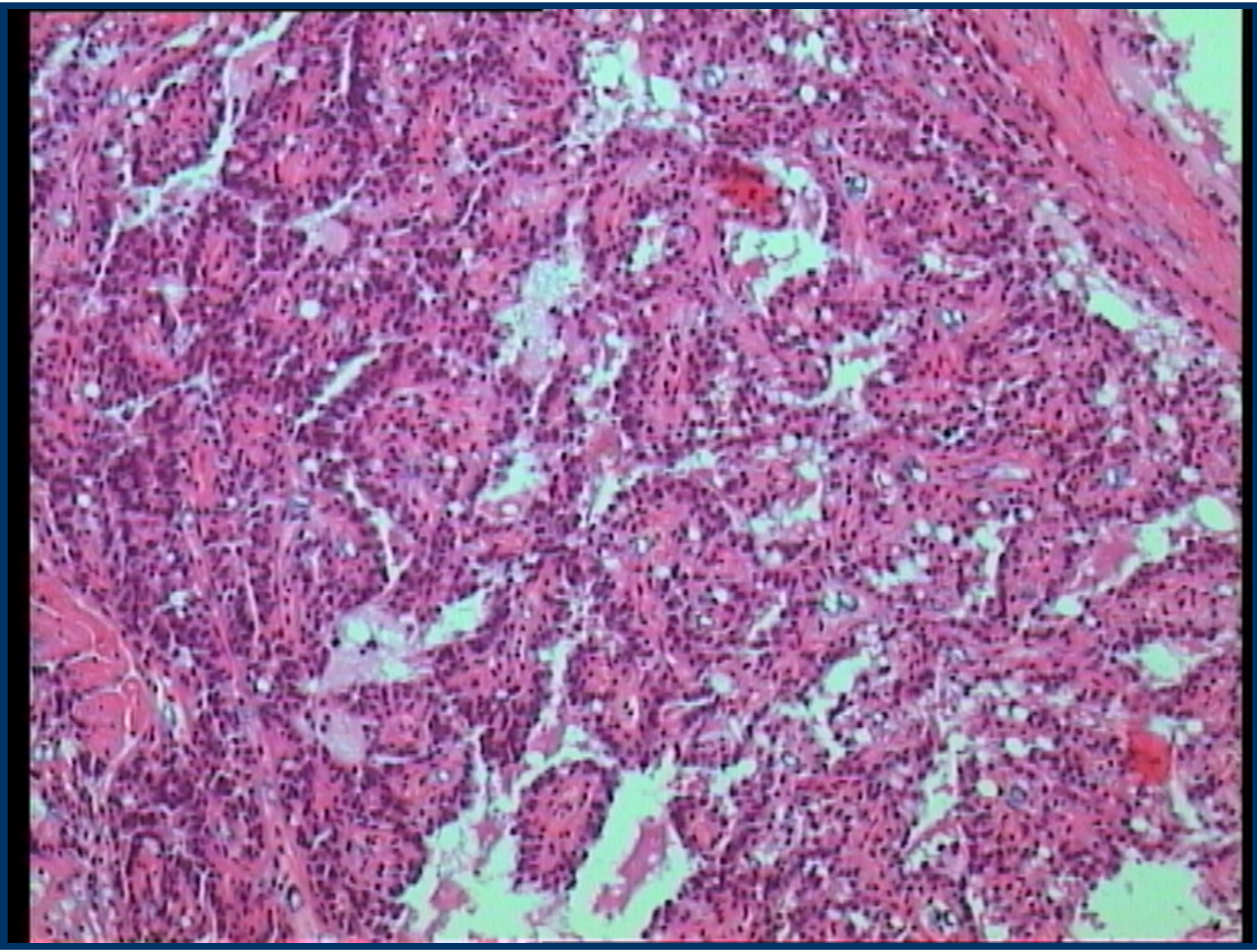
Experiment on 50 Hz MF and γ-radiation exposure: mammary carcinomas plus dysplastic precursors

Females No.	Treatment		Number per 100 animals
	μT	Rad	
112	1000	10	37.5
107	20	10	25.2
270	1000	-	14.8
105	-	10	12.4
501	-	-	10.6

Experiment on 50 Hz MF and γ-radiation exposure: mammary adenocarcinoma (25X)



Experiment 3 on 50 Hz MF and γ-radiation exposure: mammary adenocarcinoma (20X)



Conclusions

- On the basis of our experimental conditions, the exposure to low dose of γ-radiation (10 rads) and to 1000 μT 50 Hz-MF for the lifespan have shown for the first time a significant increase of the incidence of mammary cancers in female Sprague-Dawley rats.
- The current exposure limits established by ICNIRP, 100 μT for general population and up to 250 μT in occupational situation deserves, in our opinion, urgent reexamination.