STATE OF CONNECTICUT

CONNECTICUT SITING COUNCIL

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May 14, 2004

TO: Parties and Intervenors

FROM: S. Derek Phelps, Executive Director

RE: **DOCKET NO. 272** - The Connecticut Light and Power Company and The United Illuminating Company application for a Certificate of Environmental Compatibility and Public Need for the construction of a new 345-kV electric transmission line and associated facilities between the Scovill Rock Switching Station in Middletown and the Norwalk Substation in Norwalk, Connecticut. This includes construction of the Beseck Switching Station in Wallingford, East Devon Substation in Milford, and Singer Substation in Bridgeport and modifications to the Scovill Rock Switching Station and the Norwalk Substation and certain interconnections.

At the evidentiary hearing on May 13, 2004, Dr. Gary L. Ginsberg provided the following documents at the request of the Connecticut Siting Council (CSC), and have been entered into the record as CSC Exhibits.

- Curriculum Vitae (CSC Exhibit 1)
- Cancer Incidence in Connecticut, 2000 (CSC Exhibit 2)
- Cancer Incidence in Connecticut, 1995-99 (CSC Exhibit 3)
- "Induction of DNA strand breaks by intermittent exposure to extremely-low-frequency electromagnetic fields in human diploid fibroblasts", by Sabine Ivancsits, et. al. 2002 (CSC Exhibit 4)

Copies are attached for your records.

SDP/laf

Enclosures

CURRICULUM VITAE

GARY L. GINSBERG, Ph.D.

Current Address

Connecticut Department of Public Health
Division of Environmental Epidemiology and Occupational Health
410 Capitol Avenue, P.O. Box 340308, Mail Stop 11CHA
Hartford, CT 06134-0308 Phone: (860) 509-7750 gary.ginsberg@po.state.ct.us

Education

B.S. (Pharmacy): State University of N.Y. at Buffalo, 1977
Ph.D. (Toxicology): University of Connecticut, 1986

Current Position and Responsibilities

CONNECTICUT DEPARTMENT OF PUBLIC HEALTH: 12/94 to Present
Position: Senior Toxicologist
Responsibilities/Experience:
Use of toxicology and risk assessment principles to evaluate human exposures to chemicals present in air, water, soil, food, and in the workplace. Provide risk assessment expertise to CTDEP and other state agencies in standard setting and site remediation projects. Develop fish consumption advisories based upon chemical contaminant levels in fish. Provide expert witness testimony on toxics issues for state's Attorney General. Manager of a cooperative agreement with USEPA to evaluate the use of pharmacokinetic modeling in developing potency factors for chemical carcinogens. Manager of an EPA-funded study of the susceptibility differences between children and adults stemming from age-related pharmacokinetic factors. Experienced with exposure and pharmacokinetic models and their use in risk assessment.

Previous Experience

TRC ENVIRONMENTAL CORPORATION: 6/90-12/94
Position: Senior Toxicologist and Laboratory Supervisor
Responsibilities/Project Experience:

Managed risk assessment and toxicology projects involving hazardous wastes, air emissions, indoor air complaints, and worker safety. Performed human inhalation clinical trials on fuel oxygenates at Yale University. Developed methodologies to evaluate dose route extrapolation of carcinogens for USEPA. Conducted ecological endangerment assessments of impacted and hazardous waste sites. Managed chemistry laboratory projects involving a variety of techniques including gas chromatography, radon, and asbestos testing.

Publications and Presentations

Ginsberg, G., Hattis, D. and Sonawane, B. (in press) Incorporating pharmacokinetic differences between children and adults in assessing children's risks to environmental toxicants. Toxicol. Appl. Pharmacol.

Ginsberg, G., Hattis, D., Russ, A. and Sonawane, B. (2004) Physiologically-based pharmacokinetic (PBPK) modeling of caffeine and theophylline in neonates and adults: implications for assessing children's risks from environmental agents. J. Toxicol. Environ. Health, Part A, 67: 297-329.

Ginsberg, G., Slikker, W., Bruckner, J. and Sonawane, B. (2003) Incorporating children's toxicokinetics into a risk framework. Environmental Health Perspect., in press.

Ginsberg, G. (2003) Assessing cancer risks from short-term exposures in children. Risk Analysis 23: 19-34.

Hattis, D., *Ginsberg, G.*, Sonawane, B., Smolenski, S., Russ, A., Kozlak, M., and Goble, R. (2003) Differences in pharmacokinetics between children and adults. II. Children's variability in drug elimination half-lives and in some parameters needed for physiologically-based pharmacokinetic modeling. Risk Analysis 23: 117-142.

Ginsberg, G., Smolenski, S., Hattis, D., and Sonawane, B. (2002) Population distribution of aldehyde dehydrogenase-2 genetic polymorphism: implications for risk assessment. Reg. Toxicol. Pharmacol., 36: 297-309.

Ginsberg, G., Hattis, D., Sonawane, B., Russ, A., Banati, P., Kozlak, M., Smolenski, S., and Goble, R. (2002) Evaluation of child/adult pharmacokinetic differences from a database derived from the therapeutic drug literature. Toxicological Sciences 66: 185-200.

Ginsberg, G., Hattis, D., and Sonawane, B. (2002) Pharmacokinetic considerations in children's risk assessment. Toxicologist 66: Abstract No. 267, Presented at Society of Toxicology Meeting, March 2002, Nashville, TN.

Ginsberg, G. and Stilwell, D. (2001) Arsenic Exposure Issues from Children's Contact with Pressure-treated Wood. ASTHO Health and Environmental Electronic Seminar, 9/6/01.

Hattis, D. and *Ginsberg, G.* (2000) Development of a Comparative Child/Adult Pharmacokinetic Database based upon the Therapeutic Drug Literature. Report to USEPA under EPA Assistance Agreement R#827195-0 , Oct. 2000.

Ginsberg, G.L., Hattis, D., Russ, A., Banaati, P and Goble, R. (2000) Xenobiotic Metabolism and Chemical Fate from Early Childhood Onward. Presented at California EPA's Children's Environmental Health Symposium, May 2, 2000.

Ginsberg, G.L. and Toal, B.F. (2000) Development of a single meal fish consumption advisory for methyl mercury. *Risk Analysis 20: 41-47.*

Chute, S.K., *Ginsberg, G.L.*, and Pepelko, W.E. (2000) Use of pharmacokinetic modeling to relate hydrazine lung cancer potency across gavage and drinking water bioassays. Tox. Sciences 54: Abstract #881.

Ginsberg, G.L., Pelletier, D., and Toal, B. F. (1998) Risk Assessment for Manganese in Potable Water: Development of Connecticut's Draft Action Level. Presented at the May, 1998 meeting of FSTRAC (Federal and State Risk Assessment Committee), Boston, MA.

Ginsberg, G.L. and Toal, B. (1997) Mercury Fish Consumption Advisories in Connecticut. Presented at the American Fisheries Society Forum on Contaminants in Fish, December, 1997, Alexandria, Virginia.

Ginsberg, G.L., Hattis, Pelletier, D.J., Chute, S., and Pepelko, W.E. (1997) Comparison of cancer potency across dose routes: case studies with chloroform, vinyl chloride, and epichlorohydrin. Fund. Appl. Toxicol. 36, No. 1, Part 2: Abstract No. 865.

Rao, H.V. and *Ginsberg, G.L.* (1997) A physiologically based pharmacokinetic model assessment of methyl t-butyl ether in groundwater for a bathing and showering determination. Risk Analysis 17: 583-598.

Ginsberg, G.L., Pepelko, W.E., Goble, R.L., and Hattis, D.B. (1996) Comparison of contact site potency across dose routes: case study with epichlorohydrin. Risk Analysis 16: 667-681.

Cain, W.S., Leaderer, B.P., *Ginsberg, G.L.*, Andrews, L.S., Cometto-Muniz, J.E., Gent, J.F., Buck, M., Berglund, L.G., Mohensin, V., Monahan, E., and Kjaergaard, S. (1996) Acute exposure to low-level methyl tertiary butyl ether (MTBE): human reactions and pharmacokinetic response. Inhalation Toxicol. 8:21-48.

Christopher, S.M., Myers, R.C., Fowler, E.H., and *Ginsberg, G.L.* (1995) Comparative acute toxicity and irritancy of 2 chemical formulations containing N,N,N',N',-tetra-methylethylenediamine (TMEDA). Toxicologist 15:101.

Ginsberg, G.L., Goble, R.L., and Hattis, D.B. (1995) Slope factor comparison across dose routes: case study with epichlorohydrin. EPA/600/R-95/102.

Cha, S.S., *Ginsberg, G.L.*, and Guth, D.J. (1993) Odor thresholds in relation to risk assessment. Presented at the 1993 Air and Waste Management Association Meeting, Paper No. A973.

Ginsberg, G.L. (1992) Data gaps and the Clean Air Act Amendment: How will we calculate residual risk? Presented at the Boston Risk Assessment Group, Nov. 1992.

Koch, W.H., Hoffnagle, G.F., and *Ginsberg, G.L.* (1992) Burning oil fields in Kuwait: Possible inhalation risks to U.S. employees stationed in Kuwait City. Toxicologist 11:1183.

Ginsberg, G.L., Koch, W.H., Freshman, J.S., Menzie, C.A., and Deschaine, L. (1991) Migration of VOCs from ground water into buildings: an analysis of human exposure and risk. Presented at the International Symposium on the Health Effects of Gasoline, Nov. 1991, Miami, FL.

Ginsberg, G.L., Hauchman, F.S., Vetrano, K.M., Bement, C.L., and Koch, W.H. (1991) The feasibility of route-to-route extrapolation of cancer potency factors for aniline, dioxane, isophorone, and benzyl chloride. Toxicologist 10:903.

Birge, R.B., Bulera, S.J., Bartolone, J.B., Cohen, S.D., *Ginsberg, G.L.*, and Khairallah, E.A. (1991) The arylation of microsomal membrane proteins by acetaminophen is associated with the release of a 44KD acetaminophen-binding protein complex in the cytosol. Toxicol. Appl. Pharmacol. 109:443-454.

Ginsberg, G.L. and Atherholt, T.B. (1990) DNA adduct formation in mouse tissues in relation to serum levels of benzo(a)pyrene-diol-epoxide after injection of benzo(a)pyrene or the diol-epoxide. Cancer Research 50:1189-1194.

Ginsberg, G.L. and Atherholt, T.B. (1989) Transport of DNA-adducting metabolites in mouse serum following benzo(a)pyrene administration. Carcinogenesis 10:673-679.

Ginsberg, G.L., Atherholt, T.B., and Butler, G.H. (1989) Benzo(a)pyrene-induced immunotoxicity: comparison to DNA adduct formation in vivo, in cultured splenocytes, and in microsomal systems. J. Tox. Env. Health 28:205-220.

Placke, M.E., *Ginsberg, G.L.,* Wyand, D.S., and Cohen, S.D. (1987) Ultrastructural changes during acute acetaminophen-induced hepatotoxicity in the mouse: a time and dose study. Toxicologic Pathology 15:431-438.

Ginsberg, G.L., Placke, M.E., Wyand, D.S., and Cohen, S.D. (1982) Protection against acetaminophen-induced hepatotoxicity by prior treatment with fenitrothion. Toxicol. Appl. Pharmacol. 66:383-399.

(updated 3/03)

Previous Experience (cont.)

CORIELL INSTITUTE FOR MEDICAL RESEARCH: 11/86-5/90
Position: Post-Doctoral Fellow/Staff Scientist
Responsibilities:

Conducted basic research into mechanisms of chemical-induced carcinogenesis, using genetic assays to detect DNA damage (Ames Test, single strand breaks, ^{32}P-postlabeling for DNA adducts, sister chromatid exchange). Assessed the amount of genetic harm caused by agents such as cigarette smoke, chemicals leached from Superfund sites, radon, ethylene oxide, and pesticides. Evaluated molecular dosimetry techniques for potential use as human biomarkers.

UNIROYAL CHEMICAL COMPANY: 11/84-9/86
Position: Toxicologist
Responsibilities:

Designed and monitored toxicity tests for pesticides. This included tests of carcinogenicity, reproductive toxicity, acute lethality, irritation, and fish and wildlife toxicty. All tests were designed to conform with USEPA (FIFRA) guidelines.

UNIVERSITY OF CONNECTICUT: 6/79-5/86
Position: Graduate Research and Teaching Assistant
Responsibilities:

Taught undergraduate lectures and laboratory sections in pharmacology and toxicology. Conducted research into mechanisms of liver toxicity caused by drugs, solvents, and related chemicals.

Professional Activities

Adjunct Faculty: Yale University, School of Medicine, 1993-2004
Assistant Clinical Professor, Univ. of Connecticut School of Medicine, 1999-2004
Chair, Peer Review Committee for USEPA's RfD for Methylmercury, Washington, DC, 12/00
Member, USEPA's Scientific Advisory Panel for CCA-treated Wood, Washington, DC, 10/01
Member, CERHR Expert Panel on Ethylene Glycol/Propylene Glycol, Alexandria, VA, 2/03
Member, National Children's Health Study, Medicines/Pharmaceuticals Work Group, 2002-2004
Member, Massachusetts DEP Expert Panel on Proposed Perchlorate RfD, 2003
Society Memberships:

Society of Toxicology
Society for Risk Analysis

Recipient: Governor's Service Award (11/99) for training Local Health Depts in Toxic Hazards

CANCER INCIDENCE IN CONNECTICUT, 2000

CONNECTICUT TUMOR REGISTRY
CONNECTICUT DEPARTMENT OF PUBLIC HEALTH
P. O. BOX 340308
410 CAPITOL AVENUE
HARTFORD CT 06134

February, 2003

This work was supported in part by Contract N01-CN-67005 between the National Cancer Institute and the Connecticut Department of Public Health.

Requests for further information, and questions about this report, should be directed to A. P. Polednak, PhD, at the Connecticut Tumor Registry (telephone 860-509-7163)

Notes: All rates are per 100,000 (males or females in the Connecticut population, from the 2000 Census). Data shown are for invasive cancers only, except that "in situ" bladder cancers are re-coded as invasive, following standard procedures of the National Cancer Institute's SEER (Surveillance, Epidemiology and End Results) Program.

Invasive Cancers, Males, 2000

Males, 2000	Age 0-4		Age 5-9		Age 10-14		Age 15-19	
Site/type	No.	Rate	No.	Rate	No.	Rate	No.	Rate
All invasive	34	29.8	21	16.8	14	11.3	28	25.2
Lymphoma								
Hodgkin	0	.0	1	.8	2	1.6	5	4.5
Non-Hodgkin	1	.9	2	1.6	2	1.6	7	6.3
Oral,pharynx	0	.0	0	.0	0	.0	0	.0
Esophagus	0	.0	0	.0	0	.0	0	.0
Stomach	0	.0	0	.0	0	.0	0	.0
Colon	0	.0	0	.0	0	.0	0	.0
Rectum	0	.0	0	.0	0	.0	0	.0
Liver	1	.9	0	.0	0	.0	0	.0
Gallbladder	0	.0	0	.0	0	.0	0	.0
Pancreas	0	.0	0	.0	0	.0	0	.0
Larynx	0	.0	0	.0	0	.0	0	.0
Lung	0	.0	0	.0	0	.0	1	.9
Connective tissue	1	.9	1	.8	2	1.6	1	.9
Melanoma, skin	2	1.8	0	.0	0	.0	0	.0
Prostate	0	.0	0	.0	0	.0	0	.0
Testis	0	.0	0	.0	1	.8	3	2.7
Bladder	0	.0	0	.0	0	.0	0	.0
Kidney	2	1.8	1	.8	1	.8	0	.0
Brain, CNS	7	6.1	4	3.2	1	.8	4	3.6
Thyroid	0	.0	0	.0	0	.0	1	.9
Multiple myeloma	0	.0	0	.0	0	.0	0	.0
Leukemia	15	13.1	10	8.0	3	2.4	3	2.7
Kaposi's sarcoma	0	.0	0	.0	0	.0	0	.0
Unknown primary	0	.0	0	.0	0	.0	0	.0

CNS: Central Nervous System (see Appendix for codes).
All rates are per 100,000 (males) in Connecticut population in the 2000 Census.

Males, 2000	Age 20-24		Age 25-29		Age 30-34		Age 35-39	
Site/type	No.	Rate	No.	Rate	No.	Rate	No.	Rate
All invasive	35	36.8	50	50.0	82	66.8	152	106.7
Lymphoma								
Hodgkin	9	9.5	9	9.0	9	7.3	11	7.7
Non-Hodgkin	1	1.1	1	1.0	6	4.9	13	9.1
Oral,pharynx	0	.0	3	3.0	4	3.3	5	3.5
Esophagus	0	.0	0	.0	2	1.6	3	2.1
Stomach	0	.0	1	1.0	0	.0	6	4.2
Colon	0	.0	0	.0	3	2.4	6	4.2
Rectum	0	.0	0	.0	1	.8	9	6.3
Liver	2	2.1	0	.0	0	.0	2	1.4
Gallbladder	0	.0	0	.0	0	.0	0	.0
Pancreas	0	.0	0	.0	0	.0	4	2.8
Larynx	0	.0	0	.0	0	.0	2	1.4
Lung	0	.0	2	2.0	1	.8	3	2.1
Connective	3	3.2	1	1.0	5	4.1	4	2.8
Melanoma	4	4.2	1	1.0	5	4.1	20	14.0
Prostate	0	.0	1	1.0	0	.0	0	.0
Testis	6	6.3	12	12.0	16	13.0	23	16.1
Bladder	0	.0	1	1.0	1	.8	6	4.2
Kidney	0	.0	3	3.0	2	1.6	4	2.8
Brain, CNS	5	5.3	3	3.0	5	4.1	5	3.5
Thyroid	1	1.1	5	5.0	8	6.5	9	6.3
Myeloma	0	.0	0	.0	0	.0	2	1.4
Leukemia	3	3.2	6	6.0	6	4.9	6	4.2
Kaposi's	0	.0	0	.0	2	1.6	1	.7
Unknown	0	.0	0	.0	0	.0	1	.7

Males, 2000	Age 40-44		Age 45-49		Age 50-54		Age 55-59	
Site/type	No.	Rate	No.	Rate	No.	Rate	No.	Rate
All invasive	216	151.3	346	279.3	639	579.6	899	1050.0
Lymphoma								
Hodgkin	8	5.6	3	2.4	4	3.6	1	1.2
Non-Hodgkin	19	13.3	20	16.2	19	17.2	27	31.5
Oral, pharynx	15	10.5	19	15.3	26	23.6	28	32.7
Esophagus	6	4.2	7	5.7	10	9.1	11	12.9
Stomach	3	2.1	5	4.0	15	13.6	10	11.7
Colon	9	6.3	25	20.2	42	38.1	49	57.2
Rectum	11	7.7	14	11.3	29	26.3	33	38.5
Liver	4	2.8	7	5.7	10	9.1	11	12.9
Gallbladder	0	.0	2	1.6	4	3.6	2	2.3
Pancreas	4	2.8	10	8.1	12	10.9	21	24.5
Larynx	4	2.8	4	3.2	11	10.0	19	22.2
Lung	15	10.5	39	31.5	65	59.0	115	134.3
Connective tissue	6	4.2	5	4.0	7	6.4	7	8.2
Melanoma, skin	27	18.9	28	22.6	45	40.8	46	53.7
Prostate	12	8.4	47	37.9	181	164.2	343	400.6
Testis	17	11.9	18	14.5	2	1.8	4	4.7
Bladder	13	9.1	24	19.4	38	34.5	54	63.1
Kidney	8	5.6	11	8.9	32	29.0	34	39.7
Brain, CNS	6	4.2	12	9.7	11	10.0	17	19.9
Thyroid	10	7.0	10	8.1	12	10.9	6	7.0
Myeloma	3	2.1	2	1.6	14	12.7	11	12.9
Leukemia	4	2.8	13	10.5	19	17.2	18	21.0
Kaposi sarc.	1	.7	1	.8	1	.9	2	2.3
Unknown	3	2.1	7	5.7	17	15.4	14	16.4

Males, 2000	Age 60-64		Age 65-69		Age 70-74		Age 75-79	
Site/type	No.	Rate	No.	Rate	No.	Rate	No.	Rate
All invasive	1090	1745.5	1398	2586.5	1533	3069.08	1479	3588.6
Lymphoma								
Hodgkin	0	.0	5	9.3	2	4.0	1	2.4
Non-Hodgkin	44	70.5	42	77.7	49	98.1	52	126.2
Oral, pharynx	29	46.5	30	55.5	28	56.1	29	70.4
Esophagus	14	22.4	14	25.9	20	40.0	23	55.8
Stomach	25	40.1	22	40.7	37	74.1	34	82.5
Colon	74	118.6	93	172.1	149	298.3	140	339.7
Rectum	39	62.5	49	90.7	52	104.1	52	126.2
Liver	11	17.6	16	29.6	24	48.1	28	67.9
Gallbladder	1	1.6	4	7.4	3	6.0	9	21.8
Pancreas	22	35.3	24	44.4	32	64.1	32	77.6
Larynx	19	30.4	22	40.7	18	36.0	16	38.8
Lung	144	230.7	203	375.6	226	452.4	235	570.2
Connective tissue	0	.0	4	7.4	4	8.0	5	12.1
Melanoma, skin	33	52.9	44	81.4	46	92.1	54	131.0
Prostate	418	669.8	580	1073.1	578	1157.1	443	1074.9
Testis	0	.0	1	1.9	0	.0	2	4.9
Bladder	54	136.2	92	170.2	114	228.2	148	359.1
Kidney	45	72.1	51	94.4	50	100.1	38	92.2
Brain, CNS	17	27.2	18	33.3	15	30.0	12	29.1
Thyroid	3	4.8	10	18.5	1	2.0	3	7.3
Myeloma	7	11.2	16	29.6	16	32.0	22	53.4
Leukemia	27	43.3	23	42.6	27	54.1	36	87.4
Kaposi's sarc.	0	.0	2	3.7	1	2.0	1	2.4
Unknown	17	27.2	15	27.8	18	36.0	32	77.6

Males, 2000	Age 80-84		Age 85+	
Site/type	No.	Rate	No.	Rate
All invasive	974	3627.0	556	3100.6
Lymphoma				
Hodgkin	0	.0	1	5.6
Non-Hodgkin	42	156.4	18	100.4
Oral, pharynx	13	48.4	8	44.6
Esophagus	13	48.4	7	39.0
Stomach	23	85.7	19	106.0
Colon	101	376.1	80	446.1
Rectum	40	149.0	20	111.5
Liver	8	29.8	8	44.6
Gallbladder	8	29.8	5	27.9
Pancreas	22	81.9	10	55.8
Larynx	13	48.4	3	16.7
Lung	160	595.8	68	379.2
Connective tissue	6	22.3	2	11.2
Melanoma, skin	36	134.1	19	106.0
Prostate	254	945.9	136	758.4
Testis	0	.0	0	.0
Bladder	109	405.9	71	395.9
Kidney	31	115.4	11	61.3
Brain, CNS	13	48.4	3	16.7
Thyroid	1	3.7	2	11.2
Myeloma	11	41.0	8	44.6
Leukemia	22	81.9	19	105.0
Kaposi's sarc.	0	.0	2	11.2
Unknown	22	81.9	24	133.8

Males, 2000 Site/type	Total No.	Age-Standardized Rate (ASR) 1970	2000	Crude rate
All invasive	9546	509.2	608.3	578.8
Lymphoma				
Hodgkin	71	4.2	4.4	4.3
Non-Hodgkin	365	19.3	23.1	22.1
Oral, pharynx	237	12.6	14.7	14.4
Esophagus	130	6.7	8.2	7.9
Stomach	200	10.4	13.0	12.1
Colon	770	39.7	50.4	46.7
Rectum	349	18.3	22.2	21.2
Liver	132	7.0	8.4	8.0
Gallbladder	38	1.9	2.5	2.3
Pancreas	193	10.1	12.3	11.7
Larynx	131	7.1	8.2	7.9
Lung	1277	67.8	81.9	77.4
Connective tiss.	64	3.4	3.9	3.9
Melanoma, skin	410	21.2	25.6	24.9
Prostate	2993	164.3	190.4	181.5
Testis	105	5.3	6.2	6.4
Bladder	756	39.0	49.3	45.8
Kidney	324	17.6	20.3	19.6
Brain, CNS	158	9.0	9.8	9.6
Thyroid	82	4.2	4.9	5.0
Mutiple myeloma	112	5.8	7.2	6.8
Leukemia	260	14.4	16.6	15.8
Kaposi's sarcoma	14	.7	.9	.9
Unknown	170	8.6	11.2	10.3

ASR 1970 Rate: Using the total U.S. population in 1970 as the standard population in age-standardization.
ASR 2000: Using the total U.S. population in 2000 as the standard population.
The number of cancers in males divided by the total male population of Connecticut in 2000, expressed as a rate per 100,000.

Invasive Cancer, Females, 2000

	Age 0-4		Age 5-9		Age 10-14		Age 15-20	
Site/type	No.	Rate	No.	Rate	No.	Rate	No.	Rate
All invasive	20	18.3	9	7.6	25	21.2	21	19.9
Lymphoma								
Hodgkin	0	.0	1	.8	4	3.4	5	4.8
Non-Hodgkin	0	.0	0	.0	2	1.7	0	.0
Oral, pharynx	0	.0	0	.0	1	.9	0	.0
Esophagus	0	.0	0	.0	0	.0	0	.0
Stomach	0	.0	0	.0	0	.0	0	.0
Colon	0	.0	0	.0	0	.0	1	1.0
Rectum	0	.0	0	.0	0	.0	0	.0
Liver	1	.9	0	.0	0	.0	0	.0
Gallbladder	0	.0	0	.0	0	.0	0	.0
Pancreas	0	.0	0	.0	0	.0	0	.0
Larynx	0	.0	0	.0	0	.0	0	.0
Lung	0	.0	0	.0	0	.0	0	.0
Connective tissue	0	.0	0	.0	0	.0	1	1.0
Melanoma, skin	0	.0	0	.0	0	.0	2	1.9
Breast	0	.0	0	.0	0	.0	0	.0
Cervix	0	.0	0	.0	0	.0	0	.0
Corpus	0	.0	0	.0	0	.0	0	.0
Ovary	0	.0	0	.0	1	.9	2	1.9
Bladder	1	.9	0	.0	0	.0	0	.0
Kidney	4	3.7	1	.8	0	.0	0	.0
Brain, CNS	3	2.8	5	4.2	5	4.2	2	1.9
Thyroid	0	.0	0	.0	3	2.5	4	3.8
Myeloma	0	.0	0	.0	0	.0	0	.0
Leukemia	5	4.6	1	.8	5	4.2	2	1.9
Kaposi's sar.	0	.0	0	.0	0	.0	0	.0
Unknown	0	.0	0	.0	0	.0	0	.0

Females, 2000

Site/type	Age 20-24		Age 25-29		Age 30-34		Age 35-39	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate
All invasive	34	36.8	57	56.2	126	98.9	268	180.6
Lymphoma								
Hodgkin	9	9.7	3	3.0	4	3.1	7	4.7
Non-Hodgkin	1	1.1	4	3.9	4	3.1	15	10.1
Oral, pharynx	1	1.1	0	.0	2	1.6	4	2.7
Esophagus	0	.0	0	.0	0	.0	0	.0
Stomach	0	.0	0	.0	1	.8	0	.0
Colon	0	.0	0	.0	2	1.6	6	4.0
Rectum	0	.0	0	.0	1	.8	4	2.7
Liver	0	.0	0	.0	1	.8	0	.0
Gallbladder	0	.0	0	.0	0	.0	0	.0
Pancreas	0	.0	0	.0	0	.0	0	.0
Larynx	0	.0	0	.0	1	.8	0	.0
Lung	2	2.2	0	.0	2	1.6	14	9.4
Connective tissue	1	1.1	1	1.0	1	.8	4	2.7
Melanoma, skin	5	5.4	11	10.8	17	13.3	28	18.9
Breast	0	.0	7	6.9	30	23.5	103	69.4
Cervix	1	1.1	5	4.9	12	9.4	11	7.4
Corpus	1	1.1	2	2.0	4	3.1	9	6.1
Ovary	3	3.2	4	3.9	5	3.9	10	6.7
Bladder	0	.0	0	.0	0	.0	3	2.0
Kidney	0	.0	0	.0	1	.8	7	4.7
Brain, CNS	1	1.1	3	3.0	2	1.6	4	2.7
Thyroid	7	7.6	12	11.8	27	21.2	26	17.5
Myeloma	0	.0	0	.0	0	.0	1	.7
Leukemia	1	1.1	4	3.9	4	3.1	4	2.7
Kaposi's sarc	0	.0	0	.0	0	.0	0	.0
Unknown	0	.0	0	.0	2	1.6	2	1.4

Females, 2000

Site/type	Age 40-44		Age 45-49		Age 50-54		Age 55-59	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate
All invasive	419	284.2	568	440.7	775	657.8	874	956.9
Lymphoma								
Hodgkin	4	2.7	7	5.4	1	.9	3	3.3
Non-Hodgkin	14	9.5	14	10.9	23	19.5	21	23.0
Oral, pharynx	4	2.7	5	3.9	13	11.0	14	15.3
Esophagus	3	2.0	4	3.1	3	2.6	5	5.5
Stomach	1	.7	7	5.4	5	4.2	4	4.5
Colon	15	10.2	18	14.0	29	24.6	51	55.8
Rectum	2	1.4	14	10.9	22	18.7	25	27.4
Liver	1	.7	4	3.1	3	2.6	3	3.3
Gallbladder	0	.0	1	.8	4	3.4	1	1.1
Pancreas	2	1.4	6	4.7	11	9.3	21	23.0
Larynx	1	.7	2	1.6	3	2.6	3	3.3
Lung	30	20.4	24	18.6	60	50.9	125	136.9
Connective tissue	7	4.8	3	2.3	5	4.2	7	7.7
Melanoma	27	18.3	35	27.2	32	27.2	36	39.4
Breast	186	126.2	273	211.8	329	279.3	322	352.5
Cervix	19	12.9	16	12.4	11	9.3	15	16.4
Corpus	23	15.6	36	27.9	72	61.1	84	92.0
Ovary	16	10.9	26	20.2	42	35.7	33	36.1
Bladder	2	1.4	8	6.2	11	9.3	9	9.9
Kidney	7	4.8	5	3.9	19	16.1	20	21.9
Brain, CNS	11	7.5	6	4.7	6	5.1	9	9.9
Thyroid	24	16.3	28	21.7	26	22.1	18	19.7
Myeloma	1	.7	4	3.1	4	3.4	7	7.7
Leukemia	7	4.8	10	7.8	15	12.7	11	12.0
Kaposi's sar.	0	.0	0	.0	0	.0	1	1.1
Unknown	4	2.7	4	3.1	11	9.3	11	12.0

Females, 2000

Site/type	Age 60-64		Age 65-69		Age 70-74		Age 75-79	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate
All invasive	774	1117.8	923	1453.4	1094	1707.9	1226	2047.4
Lymphoma								
Hodgkin	5	7.2	1	1.6	0	.0	2	3.3
Non-Hodgkin	23	33.2	30	47.2	41	64.0	52	86.8
Oral, pharynx	7	10.1	13	20.5	24	37.5	16	26.7
Esophagus	3	4.3	4	6.3	8	12.5	9	15.0
Stomach	5	7.2	14	22.1	23	35.9	22	36.7
Colon	62	89.5	90	141.7	99	154.6	175	292.2
Rectum	22	31.8	35	55.1	42	65.6	53	88.5
Liver	7	10.1	2	3.2	7	10.9	15	25.1
Gallbladder	3	4.3	3	4.7	9	14.1	13	21.7
Pancreas	19	27.4	24	37.8	24	37.5	44	73.5
Larynx	5	7.2	5	7.9	3	4.7	2	3.3
Lung	135	195.0	159	250.4	187	291.9	205	342.3
Connective tissue	3	4.3	7	11.0	6	9.4	4	6.7
Melanoma, skin	22	31.8	18	28.3	34	53.1	24	40.1
Breast	246	355.3	276	434.6	306	477.7	306	511.0
Cervix	8	11.6	4	6.3	4	6.2	2	3.3
Corpus	74	106.9	69	108.7	63	98.4	58	96.9
Ovary	33	47.7	26	40.9	39	60.9	35	58.5
Bladder	20	28.9	36	56.7	40	62.4	45	75.2
Kidney	15	21.7	22	34.6	25	39.0	28	46.8
Brain, CNS	4	5.8	9	14.2	15	23.4	13	21.7
Thyroid	9	13.0	15	23.6	12	18.7	12	20.0
Myeloma	8	11.6	12	18.9	12	18.7	11	18.4
Leukemia	11	15.9	11	17.3	18	28.1	21	35.1
Kaposi's sar.	0	.0	0	.0	0	.0	0	.0
Unknown	15	21.7	20	31.5	26	40.6	34	56.8

Females, 2000	Age 80-84		Age 85+	
Site/type	No.	Rate	No.	Rate
All invasive	969	2088.6	884	1907.6
Lymphoma				
Hodgkin	2	4.3	3	6.5
Non-Hodgkin	37	79.8	40	86.3
Oral, pharynx	8	17.2	7	15.1
Esophagus	8	17.2	11	23.7
Stomach	18	38.8	27	58.3
Colon	148	319.0	165	356.1
Rectum	38	81.9	42	90.6
Liver	7	15.1	8	17.3
Gallbladder	11	23.7	10	21.6
Pancreas	38	81.9	37	79.8
Larynx	2	4.3	1	2.2
Lung	124	267.3	75	161.8
Connective tissue	2	4.3	5	10.8
Melanoma, skin	21	45.3	17	36.7
Breast	244	525.9	193	416.5
Cervix	9	19.4	8	17.3
Corpus	38	81.9	32	69.1
Ovary	27	58.2	21	45.3
Bladder	31	66.8	46	99.3
Kidney	21	45.3	13	28.1
Brain, CNS	12	25.9	5	10.8
Thyroid	8	17.2	4	8.6
Myeloma	17	36.6	8	17.3
Leukemia	24	51.7	28	60.4
Kaposi's sarcoma	0	.0	2	4.3
Unknown	43	92.7	51	110.1

Females, 2000		Incidence Rates:		
Site/type	Total No. No.	Age-Standardized Rate (ASR) 1970	2000	Crude Rate
All invasive	9066	373.9	444.7	516.2
Lymphoma				
Hodgkin	61	3.6	3.5	3.5
Non-Hodgkin	321	12.6	15.4	18.3
Oral, pharynx	119	5.1	6.0	6.8
Esophagus	58	2.1	2.7	3.3
Stomach	128	4.5	5.8	7.3
Colon	861	30.5	38.9	49.0
Rectum	300	11.5	14.1	17.1
Liver	59	2.3	2.8	3.4
Gallbladder	55	1.8	2.4	3.1
Pancreas	226	8.4	10.4	12.9
Larynx	28	1.3	1.4	1.6
Lung	1142	48.0	55.8	65.0
Connective tissue	57	2.5	2.9	3.3
Melanoma, skin	329	14.5	17.1	18.7
Breast	2821	119.7	141.4	160.6
Cervix	125	5.4	6.5	7.1
Corpus	565	25.3	28.6	32.2
Ovary	323	14.1	16.3	18.4
Bladder	252	9.4	11.7	14.4
Kidney	188	7.9	9.3	10.7
Brain, CNS	115	5.4	6.0	6.6
Thyroid	237	11.2	12.9	13.5
Myeloma	85	3.4	4.0	4.8
Leukemia	182	7.5	8.8	10.4
Kaposi's sarcoma	3	.1	.1	.2
Unknown	223	7.6	9.9	12.7

ASR 1970: Using the age distribution of the total U.S. population in 1970 as the standard.
ASR 2000: Using the age distribution of the total U.S. population in 2000 as the standard.
Crude Rate: Number of cancers divided by the total female population of Connecticut (2000 Census), expressed as a rate per 100,000.

APPENDIX. International Classification of Diseases for Oncology, Version 2 (ICD-O-2) Codes

Lymphomas:
Hodgkin's disease: Morphology codes 9650-9667
Non-Hodgkin's lymphoma: Morphology codes 9590-9595, 9670-9715

Others (excludes lymphomas)
ORAL, PHARYNX: C 000-149.
ESOPHAGUS: C 150-159.
STOMACH: C 160-169.
COLON: C 180-189.
RECTUM, ANUS: C 199, 209-218.
LIVER: C 220-221.
GALLBLADDER: C 239-249.
PANCREAS: C 250-259.
LARYNX: C 320-329.
TRACHEA, BRONCHUS, LUNG: C 339-349.
CONNECTIVE TISSUE: C 490-499.
MELANOMA OF SKIN: C 440-449, Morphology 8720-8799.
PROSTATE: C 619.
FEMALE BREAST: Sex female and C 500-509.
TESTIS: C 620-629.
CERVIX UTERUS: T 530-539.
UTERINE CORPUS, AND UTERUS NOT OTHERWISE SPECIFIED: C 540-549. 559.
OVARY, ADJACENT STRUCTURES: C 569-578.
BLADDER: C 670-679.
KIDNEY, RENAL PELVIS, URETER: C 649-669.
BRAIN, CEREBRAL MENINGES, CRANIAL NERVES: C 700-719, 723-725.
THYROID: C 739.
MULTIPLE MYELOMA: Morphology 9731-9732.
LEUKEMIA: Morphology 9800-9941.
KAPOSI'S SARCOMA: Morphology 9140.
UNKNOWN SITE: C 760-768, 800-809

CANCER INCIDENCE IN CONNECTICUT, 1995-99

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INTRODUCTION

This report is an update of previous reports from the Connecticut Tumor Registry on cancer incidence for five-year time periods. As in previous reports, data shown in this report are for invasive cancers, except for bladder. Non-invasive ("in situ") bladder cancers have been re-coded as invasive, following standard procedures of the National Cancer Institute's SEER (Surveillance, Epidemiology and End Results) Program.

For all tables in this report, estimates of the Connecticut population by age and sex are from U.S. Bureau of the Census estimates made in 2000. These estimates are also being used by the National Cancer Institute for the time period 1995-99, until revised estimated (based on the Year 2000 Census) are available. Use of revised population estimates will result in slightly lower cancer incidence rates.

The database of the Connecticut Tumor Registry is continously updated, due to delayed reporting of cancers to the Registry. Incidence rates are revised periodically.

AGE-STANDARDIZED CANCER INCIDENCE RATES: MALES, 1980-99

Table 1. Average Annual Age-Standardized Incidence Rates per 100,000 per Year in Connecticut Residents in 1980-84, 1985-89, 1990-94, and 1995-99

Site	1980-84 Rate/yr.	1985-89 Rate/yr.	1990-94 Rate/yr.	1995-99 Rate/yr
Lymphomas:				
Hodgkin's disease	4.1	4.1	3.9	3.5
Non-Hodgkin's lymphoma	13.9	16.3	19.1	21.1
Excluding lymphomas:				
Oral, pharynx	18.1	16.7	15.5	14.1
Esophagus	7.2	7.8	7.4	8.1
Stomach	14.2	12.9	12.0	10.8
Colon	48.7	47.8	42.8	39.1
Rectum	22.7	22.6	19.1	18.5
Liver, ducts	3.5	4.3	5.0	6.1
Gallbladder	2.4	2.4	1.9	2.2
Pancreas	11.2	11.0	10.4	11.3
Larynx	10.1	9.0	8.5	7.7
Lung	85.4	85.2	79.1	76.0
Connective Tissue	2.8	2.6	2.5	3.3
Melanoma of skin	11.3	14.1	18.2	22.0
Prostate	71.3	77.3	138.7	143.1
Testis	4.4	4.2	4.8	5.3
Bladder	34.7	36.1	35.8	36.5
Kidney	12.4	13.3	13.8	15.7
Brain, CNS	7.3	7.7	7.7	7.3
Thyroid	2.0	2.1	2.7	3.5
Multiple myeloma	4.6	4.3	5.0	5.6
Leukemia	14.1	13.3	12.3	13.6
Kaposi's sarcoma	0.7	2.2	2.5	1.3
Unknown	14.0	14.3	12.3	10.5
All	431.6	441.8	493.4	498.0
No. of cancers	33,074	36,678	43,153	44,801

Note: Rates are standardized to the 1970 U.S. population.
Data include only invasive cancers except for bladder ("in situ" bladder cancers are included).
See Appendix for ICD-O-2 codes (International Classification Of Diseases for Oncology, Version 2).

AGE-STANDARDIZED INCIDENCE RATES: FEMALES, 1980-99

Table 2. Average Annual Age-Standardized Incidence Rates per 100,000 per Year in Connecticut Residents in 1980-84, 1985-89, 1990-94, and 1995-99

	1980-84 Rate/yr.	1985-89 Rate/yr.	1990-94 Rate/yr.	1995-99 Rate/yr.
Lymphomas				
Hodgkin's disease	2.8	3.0	3.3	3.1
Non-Hodgkin's lymphoma	10.6	12.6	12.9	14.9
Excluding lymphomas:				
Oral, pharynx	7.0	6.3	6.2	5.7
Esophagus	2.1	2.1	2.0	2.1
Stomach	5.8	5.4	5.5	4.6
Colon	36.2	33.9	30.3	30.8
Rectum	13.3	12.4	11.4	12.1
Liver, ducts	1.5	1.3	1.5	2.1
Gallbladder	2.3	2.4	2.3	1.9
Pancreas	8.3	8.4	7.9	8.6
Larynx	1.8	2.0	1.9	2.1
Lung	33.1	40.6	45.3	49.4
Connective tissue	2.1	1.7	1.8	2.8
Melanoma of skin	8.9	10.7	12.5	14.4
Breast	97.5	112.4	115.9	124.3
Cervix	8.1	7.9	7.4	7.5
Corpus	23.1	20.6	23.5	24.9
Ovary	14.2	14.4	15.3	14.9
Bladder	9.1	9.2	9.8	10.5
Kidney	5.0	5.9	7.0	7.7
Brain, CNS	5.4	5.3	5.3	5.0
Thyroid	4.7	4.5	6.0	7.7
Multiple myeloma	3.3	3.4	3.2	3.8
Leukemia	8.3	7.8	7.5	8.4
Unknown	11.3	10.1	9.9	8.5
All	335.1	353.4	363.2	387.3
No. of cancers	34,764	38,812	41,300	44,709

Note: Rate are standardized to the 1970 U.S. population.
Data include only invasive cancers except for bladder ("in situ" bladder cancers are included).
See Appendix for ICD-O-2 codes.

Males: Numbers of Cancers Diagnosed 1995-99, and Average Annual Incidence Rates per 100,000 Males per Year, by Age Group

Site/type	Age 0-4 No.	Age 0-4 Rate	Age 5-9 No.	Age 5-9 Rate	Age 10-14 No.	Age 10-14 Rate	Age 15-19 No.	Age 15-19 Rate
All	123	21.9	74	12.3	67	11.8	98	18.9
Lymphoma								
Hodgkin	2	.4	1	.2	7	1.2	16	3.1
Non-Hodgkin	3	.5	8	1.3	9	1.6	14	2.7
Oral, pharynx	0	.0	0	.0	2	.4	1	.2
Esophagus	0	.0	0	.0	0	.0	0	.0
Stomach	0	.0	0	.0	0	.0	0	.0
Colon	0	.0	0	.0	1	.2	0	.0
Rectum	0	.0	0	.0	0	.0	1	.2
Liver	4	.7	1	.2	0	.0	1	.2
Gallbladder	1	.2	0	.0	0	.0	0	.0
Pancreas	0	.0	0	.0	0	.0	0	.0
Larynx	0	.0	0	.0	0	.0	0	.0
Lung	1	.2	0	.0	1	.2	0	.0
Connective tissue	11	2.0	3	.5	7	1.2	4	.8
Melanoma	0	.0	1	.2	1	.2	10	1.9
Prostate	0	.0	0	.0	0	.0	0	.0
Testis	4	.7	1	.2	0	.0	21	4.0
Bladder	0	.0	0	.0	0	.0	1	.2
Kidney	11	2.0	1	.2	0	.0	0	.0
Brain, CNS	26	4.6	19	3.2	13	2.3	6	1.2
Thyroid	0	.0	1	.2	0	.0	3	.6
Myeloma	0	.0	0	.0	0	.0	0	.0
Leukemia	38	6.8	22	3.7	16	2.8	10	1.9
Kaposi sarc.	0	.0	0	.0	0	.0	0	.0
Unknown	2	.4	1	.2	0	.0	0	.0

Males: Numbers of Cancers Diagnosed 1995-99, and Average Annual Incidence Rates per 100,000 Males per Year, by Age Group

Site/type	Age 20-24 No.	Age 20-24 Rate	Age 25-29 No.	Age 25-29 Rate	Age 30-34 No.	Age 30-34 Rate	Age 35-39 No.	Age 35-39 Rate
All	180	38.6	305	56.7	446	67.2	668	92.6
Lymphoma								
Hodgkin	28	6.0	37	6.9	28	4.2	22	3.1
Non-Hodgkin	20	4.3	31	5.8	54	8.1	76	10.5
Oral,pharynx	7	1.5	4	.7	12	1.8	28	3.9
Esophagus	0	.0	0	.0	2	.3	7	1.0
Stomach	0	.0	1	.2	0	.0	6	.8
Colon	2	.4	9	1.7	22	3.3	36	5.0
Rectum	0	.0	1	.2	8	1.2	20	2.8
Liver	0	.0	0	.0	1	.2	4	.6
Gallbladder	0	.0	0	.0	0	.0	3	.4
Pancreas	0	.0	0	.0	5	.8	8	1.1
Larynx	1	.2	0	.0	2	.3	4	.6
Lung	1	.2	2	.4	11	1.7	35	4.9
Connective tissue	6	1.3	8	1.5	12	1.8	12	1.7
Melanoma	18	3.9	30	5.6	43	6.5	95	13.2
Prostate	0	.0	0	.0	1	.2	6	.8
Testis	44	9.4	84	15.6	94	14.2	89	12.3
Bladder	2	.4	1	.2	10	1.5	20	2.8
Kidney	0	.0	1	.2	16	2.4	23	3.2
Brain, CNS	9	1.9	20	3.7	31	4.7	39	5.4
Thyroid	5	1.1	25	4.6	21	3.2	29	4.0
Myeloma	0	.0	0	.0	0	.0	11	1.5
Leukemia	20	4.3	19	3.5	21	3.2	33	4.6
Kaposi's sar.	2	.4	9	1.7	27	4.1	24	3.3
Unknown	2	.4	3	.6	4	.6	9	1.3

Males: Numbers of Cancers Diagnosed 1995-99, and Average Annual Incidence Rates per 100,000 Males per Year, by Age Group

Site/type	Age 40-44 No.	Age 40-44 Rate	Age 45-49 No.	Age 45-49 Rate	Age 50-54 No.	Age 50-54 Rate	Age 55-59 No.	Age 55-59 Rate
All	1053	160.4	1606	285.8	2751	579.9	3737	1036.7
Lymphoma								
Hodgkin	31	4.7	32	5.7	14	3.0	14	3.9
Non-Hodgkin	131	20.0	113	20.1	154	32.5	152	42.1
Oral,pharynx	46	7.0	108	19.2	140	29.5	165	45.8
Esophagus	19	2.9	31	5.5	54	11.4	90	25.0
Stomach	25	3.8	36	6.4	64	13.5	68	18.9
Colon	67	10.2	92	16.4	174	36.7	227	63.0
Rectum	31	4.7	74	13.2	125	26.4	133	36.9
Liver	10	1.5	36	6.4	41	8.6	57	15.8
Gallbladder	1	.2	5	.9	2	.4	13	3.6
Pancreas	25	3.8	39	6.9	70	14.8	91	25.3
Larynx	18	2.7	36	6.4	62	13.1	69	19.1
Lung	105	16.0	187	33.3	366	77.2	566	157.0
Connective tissue	16	2.4	20	3.6	19	4.0	15	4.2
Melanoma	132	20.1	150	26.7	196	41.3	180	49.9
Prostate	27	4.1	185	32.9	660	139.1	1165	323.2
Testis	68	10.4	37	6.6	21	4.4	9	2.5
Bladder	55	8.4	111	19.8	170	35.8	230	63.8
Kidney	50	7.6	80	14.2	112	23.6	148	41.1
Brain, CNS	31	4.7	38	6.8	51	10.8	50	13.9
Thyroid	32	4.9	41	7.3	28	5.9	28	7.8
Myeloma	10	1.5	17	3.0	36	7.6	43	11.9
Leukemia	42	6.4	50	8.9	60	12.7	69	19.1
Kaposi sarcoma	14	2.1	7	1.3	11	2.3	4	1.1
Unknown	25	3.8	35	6.2	52	11.0	67	18.6

Males: Numbers of Cancers Diagnosed 1995-99, and Average Annual Incidence Rates per 100,000 Males per Year, by Age Group

Site/type	Age 60-64 No.	Age 60-64 Rate	Age 65-69 No.	Age 65-69 Rate	Age 70-74 No.	Age 70-74 Rate	Age 75-79 No.	Age 75-79 Rate
All	5102	1735.9	7006	2461.6	7655	3046.6	6592	3228.8
Lymphoma								
Hodgkin	15	5.1	9	3.2	14	5.6	14	6.9
Non-Hodgkin	154	52.4	220	77.3	251	99.9	258	126.4
Oral, pharynx	143	48.7	160	56.2	170	67.7	124	60.7
Esophagus	88	29.9	118	41.5	110	43.8	95	46.5
Stomach	96	32.7	130	45.7	173	68.9	183	89.6
Colon	343	116.7	510	179.2	609	242.4	655	320.8
Rectum	179	60.9	254	89.2	301	119.8	226	110.7
Liver	78	26.5	68	23.9	88	35.0	77	37.7
Gallbladder	18	6.1	28	9.8	32	12.7	41	20.1
Pancreas	104	35.4	155	54.5	161	64.1	149	73.0
Larynx	82	27.9	133	46.7	106	42.2	80	39.2
Lung	855	290.9	1191	418.5	1251	497.9	1131	554.0
Connective	33	11.2	27	9.5	30	11.9	33	16.2
Melanoma	214	72.8	232	81.5	249	99.1	208	101.9
Prostate	1751	595.8	2472	868.6	2679	1066.2	1939	949.7
Testis	3	1.0	4	1.4	3	1.2	2	1.0
Bladder	341	116.0	516	181.3	575	228.9	584	286.0
Kidney	173	58.9	222	78.0	205	81.6	191	93.6
Brain, CNS	51	17.4	74	26.0	57	22.7	57	27.9
Thyroid	28	9.5	25	8.8	21	8.4	17	8.3
Myeloma	50	17.0	67	23.5	89	35.4	74	36.3
Leukemia	105	35.7	144	50.6	191	76.0	156	76.4
Kaposi sarc.	4	1.4	4	1.4	4	1.6	9	4.4
Unknown	91	31.0	115	40.4	150	59.7	161	78.9

Males: Numbers of Cancers Diagnosed 1995-99,
and Average Annual Incidence Rates per 100,000
Males per Year, by Age Group

Site/type	Age 80-84		Age 85+	
	No.	Rate	No.	Rate
All	4542	3639.7	2796	3413.3
Lymphoma				
Hodgkin	6	4.8	1	1.2
Non-Hodgkin	185	148.3	98	119.6
Oral, pharynx	89	71.3	41	50.1
Esophagus	71	56.9	37	45.2
Stomach	133	106.6	89	108.7
Colon	540	432.7	366	446.8
Rectum	191	153.1	136	166.0
Liver	39	31.3	35	42.7
Gallbladder	37	29.7	30	36.6
Pancreas	146	117.0	77	94.0
Larynx	55	44.1	28	34.2
Lung	737	590.6	390	476.1
Connective tissue	24	19.2	12	14.7
Melanoma	146	117.0	81	98.9
Prostate	1094	876.7	647	789.9
Testis	0	.0	0	.0
Bladder	442	354.2	307	374.8
Kidney	115	92.2	47	57.4
Brain, CNS	42	33.7	25	30.5
Thyroid	5	4.0	3	3.7
Myeloma	80	64.1	35	42.7
Leukemia	109	87.4	104	127.0
Kaposi sarcoma	7	5.6	8	9.8
Unknown	133	106.6	135	164.8

Males: Total Numbers of Cancers 1995-99, and Average Annual Age-Standardized Rates (ASRs) per 100,000 Per Year

Site/type	Cancers	Incidence Rates		
		ASR, 1970	ASR,2000	Crude Rate
All	44801	498.0	597.0	564.7
Hodgkin	291	3.5	3.7	3.7
Non-Hodgkin	1931	21.1	25.5	24.3
Oral, pharynx	1240	14.1	16.3	15.6
Esophagus	722	8.1	9.6	9.1
Stomach	1004	10.8	13.6	12.7
Colon	3653	39.1	49.8	46.0
Rectum	1680	18.5	22.6	21.2
Liver	540	6.1	7.2	6.8
Gallbladder	211	2.2	2.9	2.7
Pancreas	1030	11.3	13.9	13.0
Larynx	676	7.7	8.9	8.5
Lung	6830	76.0	91.1	86.1
Connective tissue	292	3.3	3.8	3.7
Melanoma	1986	22.0	26.0	25.0
Prostate	12626	143.1	167.5	159.1
Testis	484	5.3	5.9	6.1
Bladder	3365	36.5	45.7	42.4
Kidney	1395	15.7	18.3	17.6
Brain, CNS	639	7.3	8.3	8.1
Thyroid	312	3.5	3.9	3.9
Myeloma	512	5.6	6.9	6.5
Leukemia	1209	13.6	16.2	15.2
Kaposi sarcoma	134	1.3	1.7	1.7
Unknown	985	10.5	13.7	12.4

ASR 1970: Using the age distribution of the total U.S. population in 1970 as the standard.
ASR 2000: Using the age distribution of the total U.S. population in 2000 as the standard.
Crude rate: Number of cancers divided by the total female population of Connecticut (2000 Census), expressed as a rate per 100,000.

Females: Numbers of Cancers Diagnosed 1995-99, and Average Annual Incidence Rates per 100,000 Females per Year, by Age Group

Site/type	Age 0-4		Age 5-9		Age 10-14		Age 15-19	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate
All	132	24.8	55	9.6	69	12.6	110	22.5
Lymphoma								
Hodgkin	0	.0	0	.0	12	2.2	25	5.1
Non-Hodgkin	3	.6	0	.0	7	1.3	7	1.4
Oral, pharynx	1	.2	0	.0	0	.0	2	.4
Esophagus	0	.0	0	.0	0	.0	0	.0
Stomach	1	.2	0	.0	1	.2	0	.0
Colon	0	.0	0	.0	0	.0	2	.4
Rectum	0	.0	0	.0	0	.0	0	.0
Liver	5	.9	0	.0	0	.0	2	.4
Gallbladder	0	.0	0	.0	0	.0	0	.0
Pancreas	0	.0	0	.0	0	.0	0	.0
Larynx	0	.0	0	.0	0	.0	0	.0
Lung	0	.0	0	.0	0	.0	2	.4
Connective	9	1.7	1	.2	6	1.1	2	.4
Melanoma	0	.0	2	.4	3	.6	7	1.4
Breast	1	.2	0	.0	1	.2	1	.2
Cervix	0	.0	0	.0	0	.0	5	1.0
Corpus	0	.0	0	.0	0	.0	0	.0
Ovary	0	.0	1	.2	1	.2	12	2.5
Bladder	1	.2	1	.2	0	.0	0	.0
Kidney	16	3.0	8	1.4	1	.2	1	.2
Brain, CNS	22	4.1	16	2.8	14	2.6	4	.8
Thyroid	0	.0	1	.2	3	.6	14	2.9
Myeloma	0	.0	0	.0	0	.0	0	.0
Leukemia	43	8.1	19	3.3	10	1.8	14	2.9
Kaposi sarc.	0	.0	0	.0	0	.0	0	.0
Unknown	2	.4	1	.2	0	.0	0	.0

Females: Numbers of Cancers Diagnosed 1995-99, and Average Annual Incidence Rates per 100,000 Females per Year, by Age Group

	Age 20-24		Age 25-29		Age 30-34		Age 35-39	
Site/Type	No.	Rate	No.	Rate	No.	Rate	No.	Rate
All	157	34.8	333	61.2	692	102.5	1250	170.4
Hodgkin	25	5.5	31	5.7	41	6.1	28	3.8
Non-Hodgkin	9	2.0	19	3.5	36	5.3	52	7.1
Oral,pharynx	3	.7	8	1.5	8	1.2	15	2.1
Stomach	0	.0	0	.0	0	.0	2	.3
Esophagus	0	.0	2	.4	6	.9	6	.8
Colon	3	.7	6	1.1	6	.9	29	4.0
Rectum	0	.0	2	.4	16	2.4	20	2.7
Liver	1	.2	0	.0	2	.3	6	.8
Gallbladder	0	.0	0	.0	0	.0	1	.1
Pancreas	0	.0	0	.0	0	.0	8	1.1
Larynx	0	.0	1	.2	1	.2	6	.8
Lung	1	.2	2	.4	12	1.8	43	5.9
Connective	6	1.3	5	.9	9	1.3	9	1.2
Melanoma	18	4.0	43	7.9	82	12.1	127	17.3
Corpus	5	1.1	54	9.9	199	29.5	477	65.0
Cervix	9	2.0	32	5.9	76	11.3	94	12.8
Corpus	0	.0	3	.6	13	1.9	28	3.8
Ovary	12	2.7	23	4.2	36	5.3	51	7.0
Bladder	0	.0	3	.6	6	.9	10	1.4
Kidney	1	.2	5	.9	5	.7	25	3.4
Brain, CNS	11	2.4	16	2.9	20	3.0	17	2.3
Thyroid	30	6.7	48	8.8	78	11.6	112	15.3
Myeloma	0	.0	0	.0	2	.3	3	.4
Leukemia	10	2.2	10	1.8	19	2.8	28	3.8
Kaposi sarc.	0	.0	0	.0	0	.0	1	.1
Unknown	2	.4	2	.4	2	.3	6	.8

Females: Numbers of Cancers Diagnosed 1995-99, and Average Annual Incidence Rates per 100,000 Females per Year, by Age Group

Site/Type	Age 40-44 No.	Age 40-44 Rate	Age 45-49 No.	Age 45-49 Rate	Age 50-54 No.	Age 50-54 Rate	Age 55-59 No.	Age 55-59 Rate
All	1914	279.1	2793	475.6	3478	693.6	3537	918.4
Lymphoma								
Hodgkin	18	2.6	14	2.4	8	1.6	11	2.9
Non-Hodgkin	52	7.6	92	15.7	107	21.3	103	26.7
Oral, pharynx	20	2.9	35	6.0	43	8.6	61	15.8
Esophagus	1	.2	6	1.0	12	2.4	21	5.5
Stomach	9	1.3	17	2.9	30	6.0	24	6.2
Colon	52	7.6	120	20.4	150	29.9	203	52.7
Rectum	42	6.1	72	12.3	74	14.8	112	29.1
Liver	4	.6	5	.9	13	2.6	11	2.9
Gallbladder	4	.6	5	.9	8	1.6	8	2.1
Pancreas	10	1.5	31	5.3	42	8.4	58	15.1
Larynx	8	1.2	11	1.9	13	2.6	22	5.7
Lung	88	12.8	200	34.1	338	67.4	443	115.0
Connective tissue	14	2.0	18	3.1	25	5.0	17	4.4
Melanoma	144	21.0	147	25.0	154	30.7	127	33.0
Breast	886	129.2	1296	220.7	1474	294.0	1310	340.1
Cervix	94	13.7	92	15.7	70	14.0	71	18.4
Corpus	90	3.1	160	27.2	326	65.0	352	91.4
Ovary	95	13.9	137	23.3	174	34.7	168	43.6
Bladder	16	2.3	38	6.5	76	15.2	75	19.5
Kidney	32	4.7	31	5.3	48	9.6	65	16.9
Brain, CNS	30	4.4	28	4.8	23	4.6	35	9.1
Thyroid	98	14.3	94	16.0	82	16.4	38	9.9
Myeloma	6	.9	14	2.4	31	6.2	29	7.5
Leukemia	25	3.7	52	8.9	40	8.0	43	11.2
Kaposi sarc.	2	.3	3	.5	1	.2	0	.0
Unknown	23	3.4	31	5.3	48	9.6	63	16.4

Females: Numbers of Cancers Diagnosed 1995-99, and Average Annual Incidence Rates per 100,000 Females per Year, by Age Group

Site/Type	Age 60-64 No.	Age 60-64 Rate	Age 65-69 No.	Age 65-69 Rate	Age 70-74 No.	Age 70-74 Rate	Age 75-79 No.	Age 75-79 Rate
All	3958	1233.7	5030	1486.3	6112	1848.6	6021	2031.4
Lymphoma								
Hodgkin	11	3.4	13	3.8	8	2.4	10	3.4
Non-Hodgkin	153	47.7	181	53.5	279	84.4	278	93.8
Oral, pharynx	68	21.2	84	24.8	74	22.4	99	33.4
Esophagus	35	10.9	29	8.6	42	12.7	36	12.2
Stomach	34	10.6	50	14.8	104	31.5	105	35.4
Colon	269	83.8	431	127.4	646	195.4	755	254.7
Rectum	130	40.5	191	56.4	211	63.8	224	75.6
Liver	18	5.6	29	8.6	41	12.4	41	13.8
Gallbladder	25	7.8	24	7.1	48	14.5	48	16.2
Pancreas	90	28.1	122	36.1	194	58.7	214	72.2
Larynx	33	10.3	35	10.3	42	12.7	24	8.1
Lung	612	190.8	905	267.4	1045	316.1	978	330.0
Connective tissue	25	7.8	33	9.8	33	10.0	26	8.8
Melanoma	123	38.3	132	39.0	136	41.1	122	41.2
Breast	1304	406.4	1474	435.5	1676	506.9	1558	525.7
Cervix	48	15.0	51	15.1	45	13.6	45	15.2
Corpus	307	95.7	335	99.0	378	114.3	303	102.2
Ovary	125	39.0	168	49.6	211	63.8	173	58.4
Bladder	132	41.1	155	45.8	190	57.5	219	73.9
Kidney	78	24.3	125	36.9	138	41.7	119	40.2
Brain, CNS	34	10.6	48	14.2	68	20.6	50	16.9
Thyroid	37	11.5	48	14.2	31	9.4	32	10.8
Myeloma	44	13.7	56	16.6	60	18.2	101	34.1
Leukemia	64	10.0	90	26.6	116	35.1	128	43.2
Kaposi sarc.	1	.3	4	1.2	3	.9	2	.7
Unknown	75	23.4	115	34.0	160	48.4	199	67.1

Females: Numbers of Cancers Diagnosed 1995-99,
and Average Annual Incidence Rates per 100,000
Females per Year, by Age Group

	Age 80-84		Age 85-89	
	No.	Rate	No.	Rate
All	4793	2223.1	4275	1988.2
Lymphoma				
Hodgkin	6	2.8	7	3.3
Non-Hodgkin	202	93.7	188	87.4
Oral, pharynx	63	29.2	68	31.6
Esophagus	30	13.9	37	17.2
Stomach	123	57.1	132	61.4
Colon	720	334.0	789	366.9
Rectum	190	88.1	200	93.0
Liver	45	20.9	37	17.2
Gallbladder	38	17.6	46	21.4
Pancreas	181	84.0	179	83.3
Larynx	14	6.5	11	5.1
Lung	679	314.9	371	172.5
Connective tiss.	33	15.3	24	11.2
Melanoma	100	46.4	90	41.9
Breast	1124	521.3	911	423.7
Cervix	32	14.8	34	15.8
Corpus	227	105.3	146	67.9
Ovary	119	55.2	106	49.3
Bladder	199	92.3	195	90.7
Kidney	108	50.1	79	36.7
Brain, CNS	41	19.0	32	14.9
Thyroid	19	8.8	17	7.9
Myeloma	73	33.9	55	25.6
Leukemia	110	51.0	116	54.0
Kaposi sarcoma	5	2.3	11	5.1
Unknown	176	81.6	255	118.6

Females, 1995-99: Total Numbers of Cancers Diagnosed and Average Annual Age-Standardized Rates (ASRs) per 100,000 Females per Year

Site/Type	Total Number	Incidence Rates ASR, 1970	ASR, 2000	Crude Rate
All	44709	387.3	460.3	530.9
Lymphoma				
Hodgkin	268	3.1	3.2	3.2
Non-Hodgkin	1768	14.9	17.9	21.0
Oral, pharynx	652	5.7	6.7	7.7
Esophagus	251	2.1	2.5	3.0
Stomach	644	4.6	6.0	7.7
Colon	4181	30.8	39.4	49.7
Rectum	1484	12.1	14.7	17.6
Liver	260	2.1	2.5	3.1
Gallbladder	255	1.9	2.4	3.0
Pancreas	1129	8.6	10.8	13.4
Larynx	221	2.1	2.3	2.6
Lung	5719	49.4	57.8	67.9
Connective tissue	295	2.8	3.1	3.5
Melanoma	1557	14.4	17.0	18.5
Breast	13751	124.3	146.4	163.3
Cervix	798	7.5	8.9	9.5
Corpus	2668	24.9	28.5	31.7
Ovary	1612	14.9	17.3	19.1
Bladder	1316	10.5	12.8	15.6
Kidney	885	7.7	9.0	10.5
Brain, CNS	509	5.0	5.5	6.0
Thyroid	782	7.7	9.0	9.3
Myeloma	474	3.8	4.7	5.6
Leukemia	937	8.4	9.6	11.1
Kaposi sarcoma	33	.2	.3	.4
Unknown	1160	8.5	10.9	13.8

ASR 1970: Using the total U.S. population in 1970 as the standard population in age-standardization.
ASR 2000: Using the total U.S. population in 2000 as the standard population
Crude rate: The number of cancers in females divided by the total female population of Connecticut in 2000, expressed as a rate per 100,000.

APPENDIX. ICD-O-2 CODES

International Classification of Diseases for Oncology, Version 2 (ICD-O-2)

Lymphomas:

Hodgkin's disease: Morphology codes 9650-9667

Non-Hodgkin's lymphoma: Morphology codes 9590-9595, 9670-9715

Others (excludes lymphomas)

ORAL, PHARYNX: C 000-149.
ESOPHAGUS: C 150-159.
STOMACH: C 160-169.
COLON: C 180-189.
RECTUM, ANUS: C 199, 209-218.
LIVER: C 220-221.
GALLBLADDER: C 239-249.
PANCREAS: C 250-259.
LARYNX: C 320-329.
TRACHEA, BRONCHUS, LUNG: C 339-349.
CONNECTIVE TISSUE: C 490-499.
MELANOMA OF SKIN: C 440-449, Morphology 8720-8799.
PROSTATE: C 619.
FEMALE BREAST: Sex female and C 500-509.
TESTIS: C 620-629.
CERVIX UTERUS: T 530-539.
UTERINE CORPUS, AND UTERUS NOT OTHERWISE SPECIFIED: C 540-549. 559.
OVARY, ADJACENT STRUCTURES: C 569-578.
BLADDER: C 670-679.
KIDNEY, RENAL PELVIS, URETER: C 649-669.
BRAIN, CEREBRAL MENINGES, CRANIAL NERVES: C 700-719, 723-725.
THYROID: C 739.
MULTIPLE MYELOMA: Morphology 9731-9732.
LEUKEMIA: Morphology 9800-9941.
KAPOSI'S SARCOMA: Morphology 9140.
UNKNOWN SITE: C 760-768, 800-809

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Induction of DNA strand breaks by intermittent exposure to extremely-low-frequency electromagnetic fields in human diploid fibroblasts

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Abstract

Results of epidemiological research show low association of electromagnetic field (EMF) with increased risk of cancerous diseases and missing dose–effect relations. An important component in assessing potential cancer risk is knowledge concerning any genotoxic effects of extremely-low-frequency-EMF (ELF-EMF).

Human diploid fibroblasts were exposed to continuous or intermittent ELF-EMF (50 Hz, sinusoidal, 24 h, 1000 μT). For evaluation of genotoxic effects in form of DNA single- (SSB) and double-strand breaks (DSB), the alkaline and the neutral comet assay were used.

In contrast to continuous ELF-EMF exposure, the application of intermittent fields reproducibly resulted in a significant increase of DNA strand break levels, mainly DSBs, as compared to non-exposed controls. The conditions of intermittence showed an impact on the induction of DNA strand breaks, producing the highest levels at 5 min field-on/10 min field-off. We also found individual differences in response to ELF-EMF as well as an evident exposure–response relationship between magnetic flux density and DNA migration in the comet assay.

Our data strongly indicate a genotoxic potential of intermittent EMF. This points to the need of further studies in vivo and consideration about environmental threshold values for ELF exposure.

Keywords: ELF-EMF; Comet assay; Intermittent exposure; 50 Hz

1. Introduction

The permanent progress of electronic industry and the increasing use of electrical appliances involve an increase in chronic exposure of people to extremely-low-frequency electromagnetic field (ELF-EMF) of various intensities and forms. Popular media and scientists have raised concerns about possible health hazards of environmental exposure to EMF, especially to 50 and 60 Hz. There are speculations that ELF-EMF can act as promoter or co-promoter of cancer. To date, numerous contradictory results regarding the carcinogenic potential of EMF have been reported in the literature. Although data from various epidemiological studies indicate that exposure to ELF-EMF may lead to an increased risk of certain types of adult and childhood cancer, including leukemia, cancer of central nervous system, and lymphoma [1–4], others [5–7] have failed to find such an association. A critical point concerning epidemiological studies, which are always retrospective investigations, is the lack of data regarding the exact dose of exposure.

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Several in vitro investigations on the biological consequences of EMF exposure effects were performed to estimate the risk of genotoxicity of EMF and to elucidate the underlying mechanisms. Knowledge concerning any genotoxic potential of EMF is an important basis for the assessment of EMF-induced cancer risk. Genotoxic effects of EMF may occur directly by damage to chromosomes or by damage to DNA repair mechanisms. Indirect genotoxic effects may arise by various processes like the generation of oxygen radicals or impairment of radical-scavenging mechanisms. Controversial results have been reported [8–11] with genotoxic endpoints as sister chromatid exchange (SCE), micronuclei (MN), chromosomal aberrations (CAs) and assessment of DNA strand breaks at exposure levels ranging from 1 μT to 10 mT. The majority of these studies did not show any EMF-related genotoxic effects. The few positive reports have not or could not be independently reproduced. An exposure–response relationship could not be demonstrated as well. However, these positive results must not be neglected.

Different in vitro exposure conditions, exposure setups, used methods and investigated targets make it difficult to compare the results for risk evaluation. Due to these facts, the REFLEX (risk evaluation of potential environmental hazards from low energy EMF exposure using sensitive in vitro methods) project was started, funded by the European Union, involving 12 independent research groups. To enable experiments under controlled and standardized conditions and to verify positive results, each of these groups was supplied with the same exposure setup, for ELF or radio frequency (rf), respectively.

Our aim of the project is to investigate possible genotoxic effects due to ELF-EMF exposure using the comet assay. To discriminate between DNA single-(SSB) and double-strand breaks (DSB), the neutral comet assay (detection of DSB) was used in addition to alkaline comet assay analysis (detection of SSB + DSB).

2. Materials and methods

2.1. ELF-EMF exposure conditions and cell culture

Human diploid fibroblasts (IH-9: 28 years of age, female; ES-1 male, 6 years of age) initiated from skin biopsies from healthy donors were maintained in culture in Dulbecco's modified Eagle's medium (DMEM, Gibco, Vienna, Austria) supplemented with 10% fetal calf serum (FCS), 20 mM Hepes buffer, 40 μg/ml neomycin, 2 mM L-glutamine, 100 IU/ml penicillin and 100 μg/ml streptomycin (Gibco, Vienna, Austria). Cells were grown in 175 cm^2 culture flasks at 37 °C in a humidified atmosphere in the presence of 5% CO_2 and were supplied with fresh culture medium every 48 h. Twenty-four hours before the start of the ELF experiments, fibroblasts were seeded into 35 mm Petri dishes at a density of 5×10^4 cells/3 ml.

The exposure system was built and provided by the IT'IS-foundation (Foundation for Information Technologies in Society, ETH, Zurich, Switzerland) within a study funded by the European Union. The setup generating a vertical EMF consisted of two four-coil systems (two coils with 56 windings, two coils with 50 windings), each of which was placed inside a μ-metal box. The currents in the bifilar coils could be switched parallel for field exposure or non-parallel for control (sham-exposure). Both systems were placed inside a commercial incubator (BBD 6220, Kendro, Vienna, Austria) to ensure constant environmental conditions (37 °C, 5% CO_2, 95% humidity). In addition, the temperature was monitored at the location of the dishes during exposure and was maintained at 36.5–37.5 °C. The temperature difference between the chambers did not exceed 0.3 °C, so possible thermal effects could be ruled out. A current source based on four audio amplifiers (Agilent Technologies, Zurich, Switzerland) allowed magnetic field up to 2.3 mT. The field could be varied in the frequency range from dc—1.5 kHz by a computer controlled function generator. To enable blinded exposures, the computer randomly determined which of the two the exposure setup was. The fields as well as all sensors in each chamber were continuously monitored. All experiments were performed at a frequency of 50 Hz sinusoidal for 24 h. To study the influence of different intermittences, the magnetic flux density was maintained at 1 mT, for studying dose–response effects, the magnetic flux density was varied between 20 and 2000 μT at a definite intermittence (5 min field-on/10 min field-off).

After exposure the fibroblasts were detached by trypsin, suspended in fresh culture medium. After

comet assay analysis, results were decoded. Each exposure level was tested in duplicate.

2.2. Comet assay analysis

We followed the technique described by Östling and Johanson [12] with minor modifications by Singh et al. [13,14]. Fully frosted microscopic slides (CMS, Houston, USA) were used.

ELF- and sham-exposed cells (10,000–30,000) were mixed with 100 μl low melting agarose (0.5%, 37 °C) to form a cell suspension, pipetted onto 0.5% normal melting agarose pre-coated slides, spread using a cover slip, and maintained on a cold flat tray for about 10 min to solidify. After removal of the cover slip the third layer of 0.5% low melting agarose was added and solidified. The slides were immersed in freshly prepared cold lysis solution (2.5 M NaCl, 100 mM Na_2EDTA, 10 mM Tris, pH 10, 1% sodium sarcosinate, 1% Triton X-100, 10% DMSO, pH 10) and lysed for 90 min at 4 °C. Subsequently, the slides were drained and placed in a horizontal gel electrophoresis tank side by side, nearest the anode. The tank was filled with fresh electrophoresis buffer (1mM Na_2EDTA, 300 mM NaOH, pH 13 in case of alkaline comet assay, and 100 mM Tris, 300 mM sodium acetate, 500 mM sodium chloride, pH 8.5 in case of neutral comet assay) to a level approximately 0.4 cm above the slides. For both, alkaline and neutral comet assays, slides were left in the solution for 40 min for equilibration and unwinding of the DNA before electrophoresis. Electrophoresis conditions (25 V, 300 mA, 4 °C, 20 min, field strength: 0.8 V/cm) were the same for neutral and alkaline comet assay. All steps were performed under dimmed light to prevent the occurrence of additional DNA damage. After electrophoresis the slides were washed three times with Tris buffer (0.4 M Tris, pH 7.5) to neutralize, then air-dried and stored until analysis. Comets were visualized by ethidium bromide staining (20 μg/ml, 30 s) and examined at 400× magnification using a fluorescence microscope (Axiophot, Zeiss, Germany). One thousand DNA spots from each sample were classified into five categories corresponding to the amount of DNA in the tail according to Anderson et al. [15] with modifications. The proposed classification system provides a fast and inexpensive method for genotoxic monitoring. Due to the classification to different groups by eye, no special imaging software is required. The different classification groups are not weighted equally, due to the fact that they do not represent equal grades of damage. Moreover, the technique becomes more sensitive, because many cells can be scored in a short time (1000 cells instead of 50–100 cells with image analyzing). The subsequent calculation of a "comet tailfactor" allows quantifying DNA damage as a single figure, which makes it easier to compare results. Due to the scoring of 1000 cells in one experiment, which are 10-fold the cells processed with image analyzing, standard deviations are very low. Reproducibility has been thoroughly checked.

Results were expressed as "comet tailfactors", calculated according to Diem and Rüdiger [16]. All analyses were performed by the same investigator. Fig. 1 shows the five classification groups with the group averages and the microphotograph.

Tailfactors were calculated according to the following formula:

$$\text{tailfactor}\,(\%) = \frac{AF_A + BF_B + CF_C + DF_D + EF_E}{1000}$$

where A is the number of cells classified to group A, F_A the average of group A (2.5), B the number of cells classified to group B, F_B the average of group B (12.5), C the number of cells classified to group C, F_C the average of group C (30), D the number of cells classified to group D, F_D is the average of group D (67.5), E the number of cells classified to group E, and F_E the average of group E (97.5).

2.3. Statistical analysis

Statistical analysis was performed with STATISTICA V. 5.0 package (Statsoft Inc., Tulsa, USA) and SPSS 10.0 package (SPSS Inc., Illinois, USA). All data are presented as mean±standard deviation (S.D.). The differences between exposed and sham-exposed, as well as between different exposure conditions were tested for significance using independent Student's t-test or one-factorial ANOVA with post-hoc Bonferroni correction. A difference at $P < 0.05$ was considered statistically significant. Correlations were assessed by multiple regression analysis using linear regression.

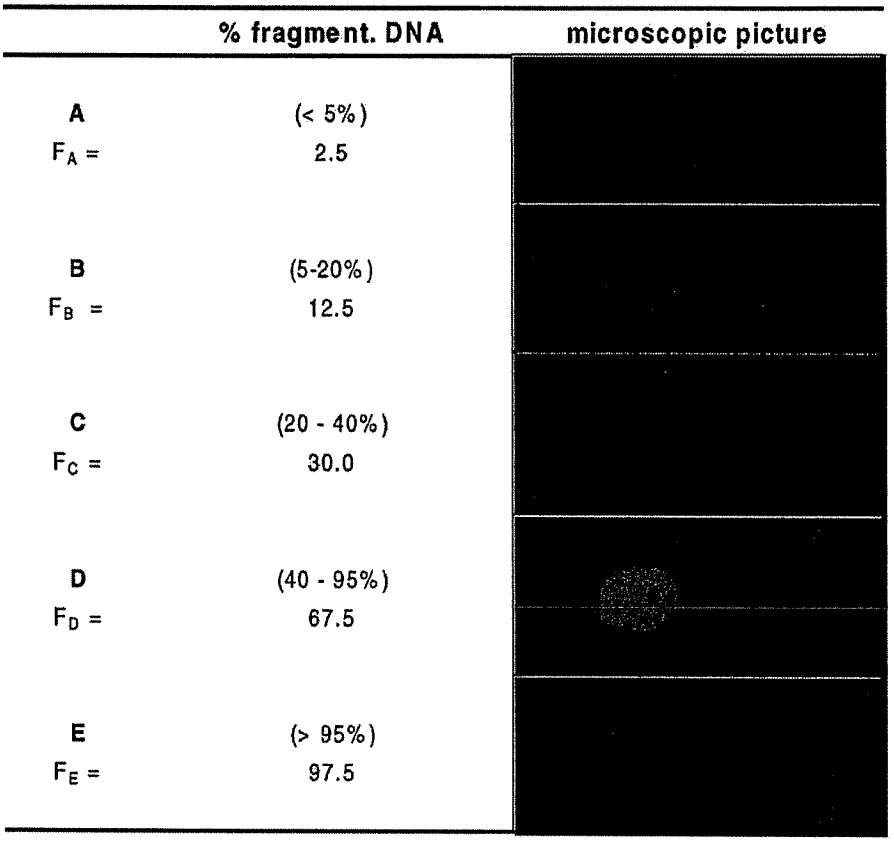

Fig. 1. Classification groups and respective microscopic appearance (cell line ES-1).

3. Results

In the first set of experiments fibroblasts were continuously exposed to ELF-EMF at 1000 μT 24 h. In these experiments we did not find any significant differences between exposed and sham-exposed cells (Tables 1 and 2) in the alkaline and neutral comet assays. As Nordenson et al. [17] reported positive genotoxic effects applying intermittent field exposure, our next experiments concentrated on exposures at different intermittence conditions. Intermittences of 5/5 and 15/15 min revealed an increase of both, alkaline and neutral comet assay levels, compared to sham-exposed cells, whereas 5 min field-on/25 min field-off failed to reproduce these results (Tables 1 and 2). On the basis of these findings, we tried to figure out the optimal exposure conditions for maximal effects on DNA strand break levels.

We started with a fixed field-on time of 5 min and varied field-off times from 5 to 25 min. These experiments indicated that DNA strand break levels (SSB and DSB) culminated at an off-time of 10 min and reached control levels at extended off-times (Fig. 2). Significant differences ($P < 0.01$) between exposed and sham-exposed cells were found at 5/5, 5/10, 5/15 and 5/20 intermittences for alkaline comet assay and at 5/5, 5/10 and 5/15 intermittences for neutral comet assay, but not at 5/25 for both assays.

Subsequently, a fixed off-time of 10 min was chosen and on-times have been varied from 1 to 25 min. Again, the highest level of DNA strand breaks was obtained at an intermittence of 5 min field-on/10 min field-off (Fig. 3). Tailfactors of exposed and sham-exposed cells differed significantly at each on-time in alkaline comet assay and at 3–15 min field-on in the

Table 1
Mean values of alkaline comet assay tailfactors at different exposure conditions ($n = 2$), cell line IH-9

Different exposure conditions	Exposed		Sham	
	Comet tailfactor (%)	±S.D.[a]	Comet tailfactor (%)	±S.D.
Continuous exposure (24 h)	4.29	0.02	4.27	0.03
15/15 on/off	6.47*	0.14	4.23	0.05
5/5 on/off	6.98*	0.04	4.41	0.16
5/10 on/off	7.47*	0.13	4.48	0.05
5/15 on/off	6.68*	0.17	4.42	0.03
5/20 on/off	5.90*	0.12	4.38	0.12
5/25 on/off	4.27	0.04	4.23	0.03
1/10 on/off	5.89*	0.19	4.21	0.14
3/10 on/off	6.60*	0.06	4.19	0.22
10/10 on/off	6.91*	0.07	4.24	0.07
15/10 on/off	6.56*	0.15	4.11	0.08
25/10 on/off	5.37*	0.05	4.21	0.04

[a] Indicates standard deviation.
* Indicates significant differences ($P < 0.05$) exposed vs. sham.

neutral comet assay. Significant differences between the tailfactors of exposed cells at various intermittence conditions are presented in Table 3 for the alkaline comet assay and in Table 4 for the neutral comet assay. Solely the alkaline comet tailfactors of 5/10, 5/25 and 25/10 EMF-exposed cells differed significantly to the other applied intermittence conditions. Since an intermittence of 5/10 was able to induce the highest levels of DNA strand breaks in both alkaline and neutral comet assays, further experiments were performed at 5/10.

Testing two different cell lines (IH-9, ES-1; 1000 μT, 24 h, 5/10), again, significant differences ($P < 0.00001$) in alkaline and neutral comet tailfactors between exposed and sham-exposed cells (Table 5, Fig. 4) as well as between exposed cells of these two strains could be found. Sham-exposed IH-9 and ES-1 cells did not differ significantly, indicating that inter-individual differences in ELF response may exist. Figs. 5 and 6 show the distribution of cells with different grades of damage in alkaline and neutral comet assays, respectively.

Table 2
Mean values of neutral comet assay tailfactors at different exposure conditions ($n = 2$), cell line IH-9

Different exposure conditions	Exposed		Sham	
	Comet tailfactor (%)	±S.D.[a]	Comet tailfactor (%)	±S.D.
Continuous exposure (24 h)	4.20	0.03	4.17	0.05
15/15 on/off	5.72*	0.01	4.25	0.04
5/5 on/off	6.09*	0.02	4.31	0.08
5/10 on/off	6.21*	0.01	4.35	0.07
5/15 on/off	5.66*	0.06	4.23	0.13
5/20 on/off	4.52	0.16	4.50	0.21
5/25 on/off	4.25	0.05	4.34	0.07
1/10 on/off	4.16	0.15	4.16	0.13
3/10 on/off	5.94*	0.05	4.20	0.06
10/10 on/off	6.19*	0.11	4.11	0.11
15/10 on/off	6.02*	0.03	4.21	0.10
25/10 on/off	5.44	0.01	4.15	0.01

[a] Indicates standard deviation.
* Indicates significant differences ($P < 0.05$) exposed vs. sham.

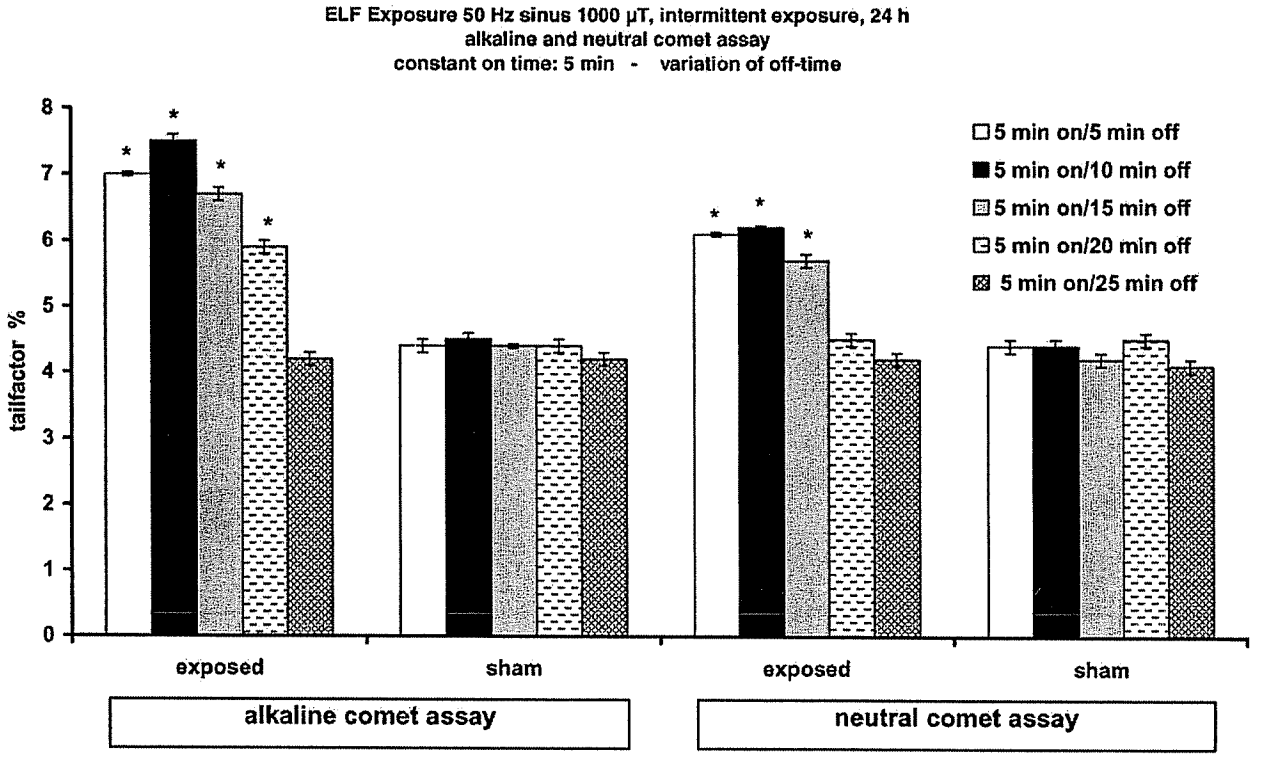

Fig. 2. Alkaline and neutral comet assay tailfactors of ELF exposed fibroblasts (cell line IH-9, 50 Hz sinus, 24 h, 1000 µT, intermittent) variation of off-time. *$P < 0.01$ exposed vs. sham-exposed.

To test the exposure–response relationship, magnetic flux density was varied between 20 and 2000 µT (at 24 h, 5/10). Even a magnetic flux density as low as 70 µT produced significantly elevated ($P < 0.01$) alkaline and neutral comet assay levels as compared to sham-exposed controls (Table 6, Fig. 7). Two plateau-like sections between 100 and 500 µT and between 1000 and 2000 µT could be revealed, which

Table 3
Significant ($P < 0.05$) differences between different intermittence conditions—alkaline comet assay

	P-values at various on/off times (min)									
	5/5	5/10	5/15	5/20	5/25	1/10	3/10	10/10	15/10	25/10
5/5	–	0.02	N.S.	<0.001	<0.001	<0.001	N.S.	N.S.	N.S.	<0.001
5/10	0.02	–	<0.001	<0.001	<0.001	<0.001	<0.001	0.007	<0.001	<0.001
5/15	N.S.	<0.001	–	<0.001	<0.001	<0.001	N.S.	N.S.	N.S.	<0.001
5/20	<0.001	<0.001	<0.001	–	<0.001	N.S.	0.001	<0.001	<0.001	0.021
5/25	<0.001	<0.001	<0.001	<0.001	–	<0.001	<0.001	<0.001	<0.001	<0.001
1/10	<0.001	<0.001	<0.001	N.S.	<0.001	–	0.001	<0.001	0.001	0.021
3/10	N.S.	<0.001	N.S.	0.001	<0.001	0.001	–	N.S.	N.S.	<0.001
10/10	N.S.	0.007	N.S.	<0.001	<0.001	<0.001	N.S.	–	N.S.	<0.001
15/10	N.S.	<0.001	N.S.	<0.001	<0.001	0.001	N.S.	N.S.	–	<0.001
25/10	<0.001	<0.001	<0.001	0.021	<0.001	0.021	<0.001	<0.001	<0.001	–

N.S.: not significant, post-hoc compared Bonferroni corrected.

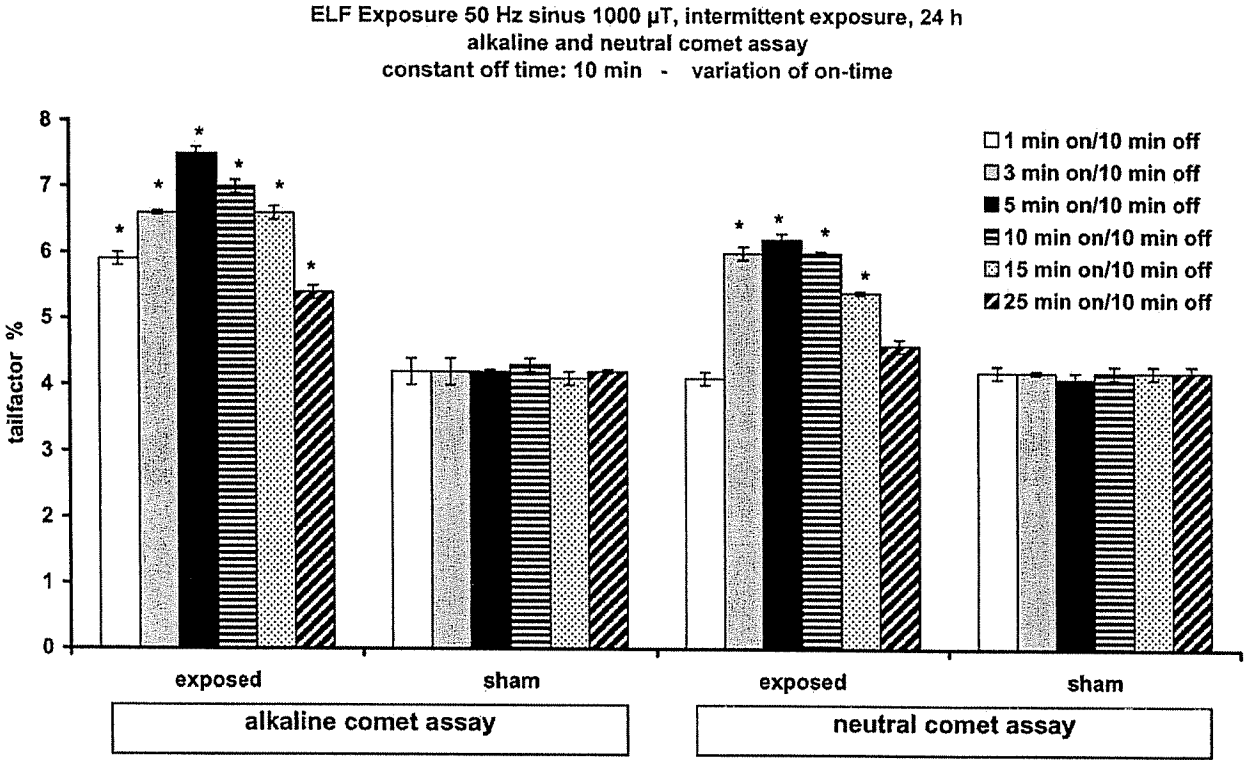

Fig. 3. Alkaline and neutral comet assay tailfactors of ELF exposed fibroblasts (cell line IH-9, 50 Hz sinus, 24 h, 1000 µT, intermittent) variation of on-time. *$P < 0.01$ exposed vs. sham exposed.

might point to a biphasic mechanism. In Fig. 8 the alkaline and neutral tailfactors are plotted versus log (magnetic flux density in µT), showing an exponential dose–response relationship. Using regression analysis, a significant correlation between comet tailfactors and applied magnetic field (alkaline comet assay: $r = 0.843$, $P = 0.004$; neutral comet assay: $r = 0.908$, $P = 0.0007$), as well as between alkaline and neutral comet assays could be found ($r = 0.974$, $P = 0.00001$).

Table 4
Significant ($P < 0.05$) differences between different intermittence conditions—neutral comet assay

	P-values at various on/off times (min)									
	5/5	5/10	5/15	5/20	5/25	1/10	3/10	10/10	15/10	25/10
5/5	–	N.S.	N.S.	<0.001	<0.001	<0.001	N.S.	N.S.	<0.001	<0.001
5/10	N.S.	–	0.007	<0.001	<0.001	<0.001	N.S.	N.S.	<0.001	<0.001
5/15	N.S.	0.007	–	<0.001	<0.001	<0.001	N.S.	N.S.	N.S.	<0.001
5/20	<0.001	<0.001	<0.001	–	N.S.	N.S.	<0.001	<0.001	<0.001	N.S.
5/25	<0.001	<0.001	<0.001	N.S.	–	N.S.	<0.001	<0.001	N.S.	N.S.
1/10	<0.001	<0.001	<0.001	N.S.	N.S.	–	<0.001	<0.001	<0.001	N.S.
3/10	N.S.	N.S.	N.S.	<0.001	<0.001	<0.001	–	N.S.	0.013	<0.001
10/10	N.S.	N.S.	N.S.	<0.001	<0.001	<0.001	N.S.	–	0.002	<0.001
15/10	<0.001	<0.001	N.S.	<0.001	N.S.	<0.001	0.013	0.002	–	<0.001
25/10	<0.001	<0.001	<0.001	N.S.	N.S.	N.S.	<0.001	<0.001	<0.001	–

N.S.: not significant, post-hoc compared Bonferroni corrected.

Table 5
Mean values of alkaline and neutral comet assay tailfactors of different cell strains (IH-9, ES-1) at intermittent ELF exposure (5/10 on/off, 1000 μT, 24 h) ($n = 10$)

	Alkaline comet assay				Neutral comet assay			
	Exposed		Sham		Exposed		Sham	
	Tailfactor (%)	±S.D.[a]	Tailfactor (%)	±S.D.	Tailfactor (%)	±S.D.	Tailfactor (%)	±S.D.
ES-1	6.50*	0.12	3.98	0.12	5.62*	0.16	3.95	0.08
IH-9	7.44*	0.09	4.12	0.12	6.53*	0.08	4.06	0.12

[a] Indicates standard deviation.
* Indicates significant differences ($P < 0.05$) exposed vs. sham.

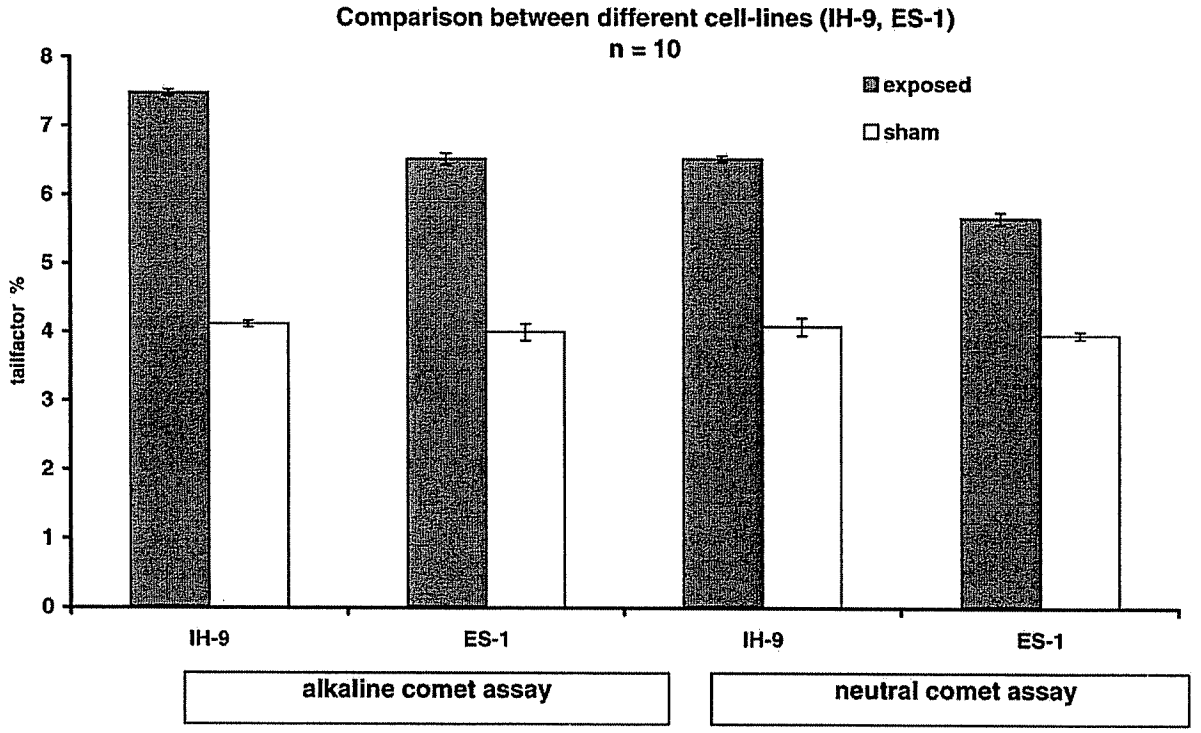

Fig. 4. Alkaline and neutral comet assay tailfactors of ELF exposed fibroblasts (50 Hz sinus, 24 h, 1000 μT, intermittent 5/10) comparison between different cell lines.

4. Discussion

Our results show, that intermittent exposure to a 50 Hz magnetic field causes a reproducible increase in DNA strand breaks in cultured human diploid fibroblasts. The majority of the studies investigating genotoxic effects of 50/60 Hz [8,9] EMF were performed at continuous exposure. Nearly all have reported a negative outcome on genotoxicity of ELF-EMF. Our results from tests with continuous exposure of fibroblasts to EMF corroborate these findings. Subjecting cells continuously to a constant field probably may induce adaptive mechanisms, protecting the genome from harmful influences. A regular change of environmental conditions might interfere with such mechanisms and lead to DNA impairment. The extent of damage would depend on the duration of exposure and the time of recovery. A proper mechanism by which magnetic fields

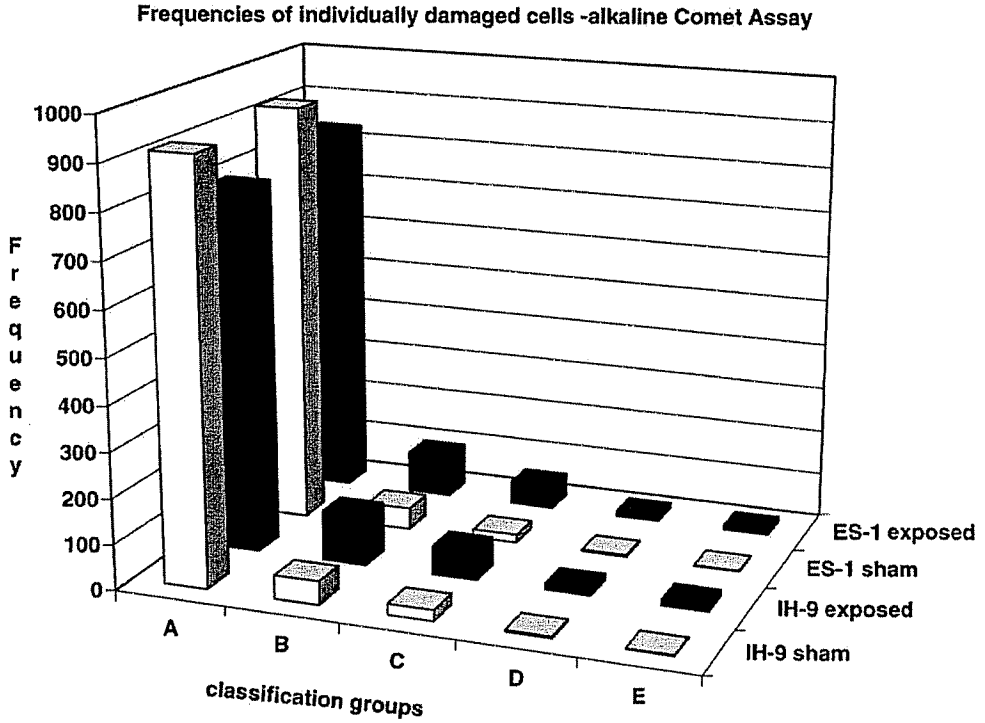

Fig. 5. Alkaline comet assay frequencies of individually damaged cells of sham- and ELF-exposed fibroblasts (50 Hz sinus, 24 h, 1000 μT, intermittent 5/10) comparison between different cell lines.

may interact with biological systems has not been found as yet. Several hypotheses like induction of electric currents [18], increased free radical activity [19] or acceleration of electron transfer in different enzymes and proteins [20] have been proposed. Although all of these theories are mostly speculative, i.e. the latter, the interaction of EMF with moving charges seems to have a plausible biophysical basis. Recent observations

Table 6
Mean values of alkaline and neutral comet tailfactors at intermittent ELF exposure (5/10 on/off, 1000 μT, 24 h) ($n = 2$) dose response, cell line ES-1

Magnetic flux density (μT)	Alkaline comet assay				Neutral comet assay			
	Exposed		Sham		Exposed		Sham	
	Tailfactor (%)	±S.D.[a]	Tailfactor (%)	±S.D.	Tailfactor (%)	±S.D.	Tailfactor (%)	±S.D.
20	4.16	0.02	4.21	0.13	3.63	0.01	3.60	0.08
50	4.16	0.06	4.20	0.12	3.70	0.16	3.72	0.03
70	4.87*	0.03	4.28	0.02	3.99*	0.01	3.71	0.01
100	5.25*	0.06	4.28	0.05	4.32*	0.00	3.73	0.04
250	5.31*	0.02	4.25	0.07	4.24*	0.06	3.60	0.02
500	5.52*	0.01	4.22	0.01	4.48*	0.02	3.79	0.05
750	6.17*	0.08	4.26	0.11	5.08*	0.08	3.67	0.10
1000	6.50*	0.18	4.27	0.10	5.71*	0.01	3.79	0.16
2000	6.62*	0.01	4.13	0.04	5.79*	0.05	3.70	0.01

[a] Indicates standard deviation.
* Indicates significant differences ($P < 0.05$) exposed vs. sham.

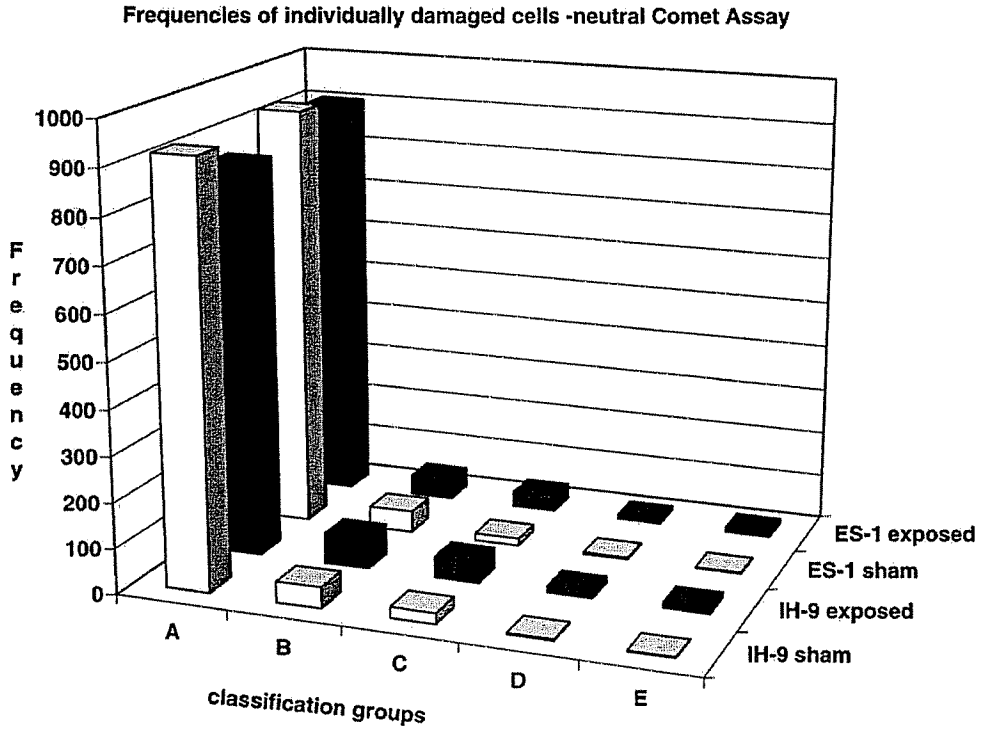

Fig. 6. Neutral comet assay frequencies of individually damaged cells of sham- and ELF-exposed fibroblasts (50 Hz sinus, 24 h, 1000 μT, intermittent 5/10) comparison between different cell lines.

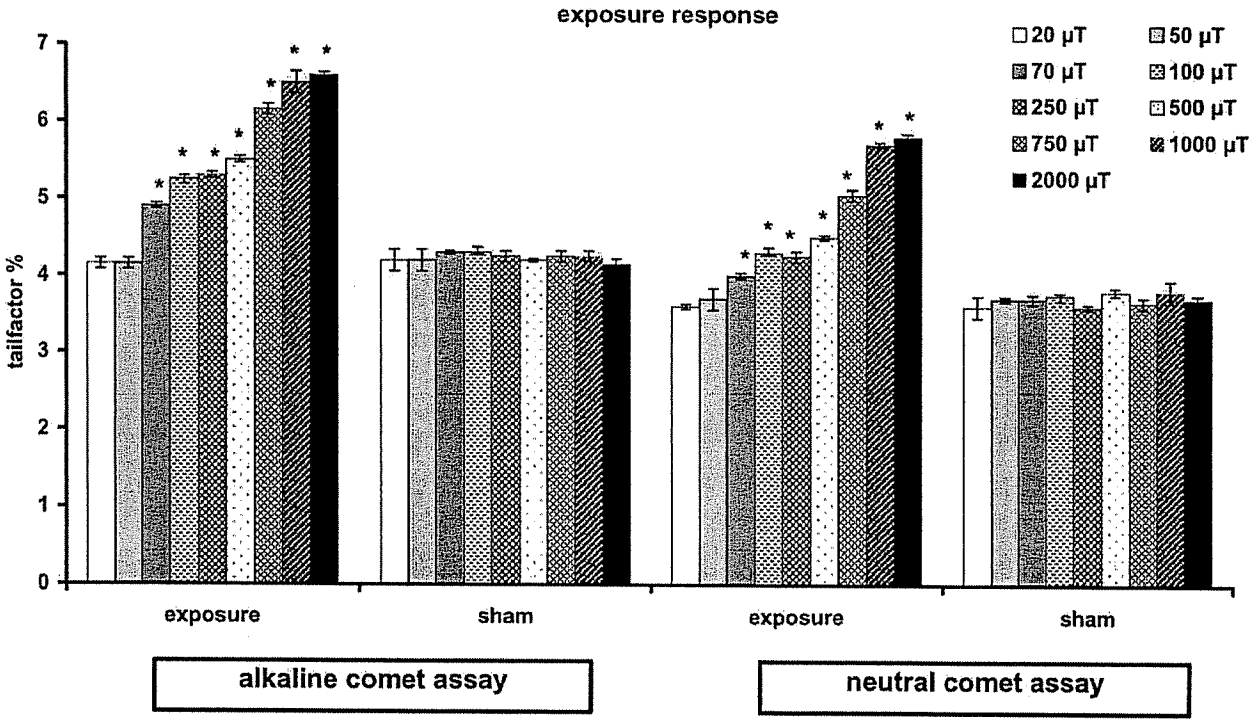

Fig. 7. Alkaline and neutral comet assay tailfactors of ELF exposed fibroblasts (ES-1, 50 Hz sinus, 24 h, 1000 μT, intermittent 5/10) exposure response. $^{*}P < 0.01$ exposed vs. sham-exposed.

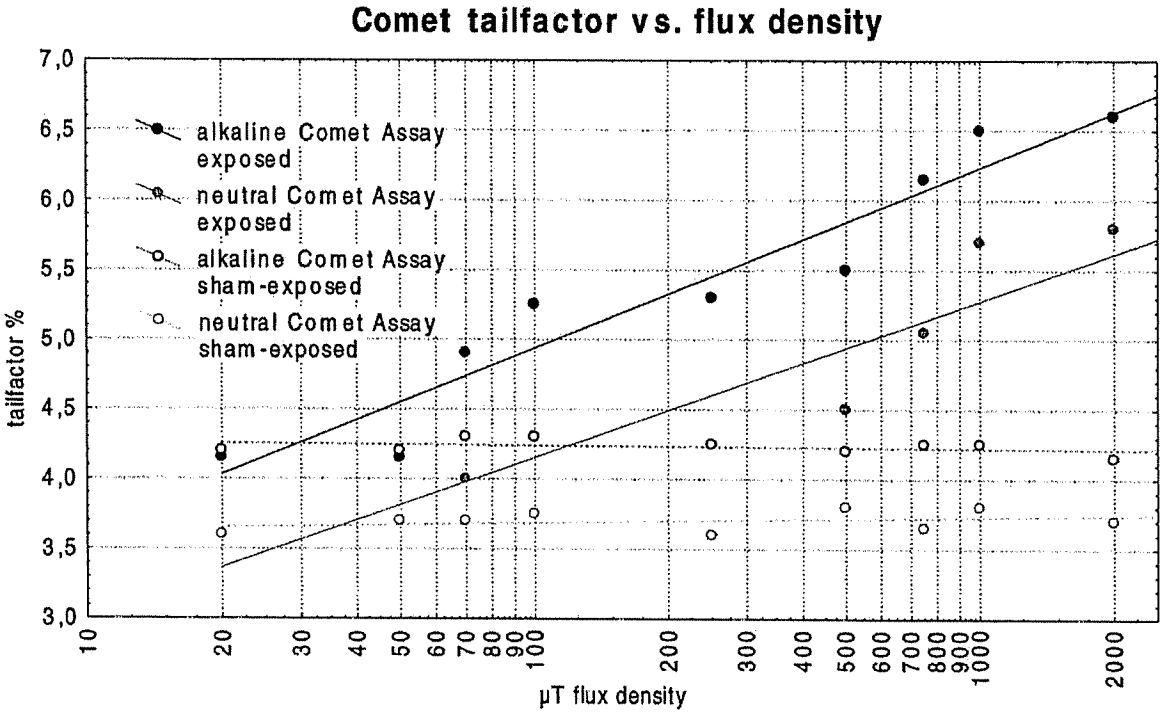

Fig. 8. Alkaline and neutral comet assay tailfactors of ELF exposed fibroblasts (cell line ES-1, 50 Hz sinus, 24 h, 1000 µT, intermittent 5/10) exposure response.

show, that DNA can transfer electrons within its base pairs [21,22]. These studies suggest that EMF may initiate transcription by interacting with moving electrons in DNA [23] by generating repulsive (Lorentz) forces causing chain separation at specific DNA sequences (*n*CTCT*n*) [24]. As within the state of transcription DNA presents a vulnerable target to genotoxic influences, the on/off switching at intermittent ELF-EMF exposure may lead to DNA disruption, causing DNA strand breaks. In our experiments the relation on- to off-time appeared to be crucial for the extent of damage caused. An intermittence of 5/10 was able to produce the highest levels of DNA strand breaks, whereas at 5/25 no significant difference to the concurrent control was found. We suppose, that at extended off-times (>15 min) ELF-induced damage could be removed by DNA repair mechanisms. This explanation is speculative and requires further assessment, e.g. evaluation of repair kinetics. However, a study conducted by Miyakoshi et al. [25] demonstrated that ELF exposure (continuous exposure, 5–400 mT, 30 min) alone did not induce DNA strand breaks in human glioma cells, but enhanced X-ray-induced DNA damage, by affecting DNA repair. These findings suggest, that ELF exposure seems to have a negative impact on DNA repair mechanisms. Therefore at intermittent exposure an extended off-time would give time for recovery.

Since we found significant differences in ELF-EMF response in different donors, individual factors like sex, or age might play an important role in the susceptibility of DNA to EMF. Regarding the distribution data (Figs. 5 and 6) in different cell lines after ELF exposure, the observed effect does not seem to be present in all cells. It is possible, that there may exist an "ELF-sensitive" fraction (e.g. cells in a specific stage of cell cycle) and that this portion of cells might vary individually.

At our experimental settings (24 h, 1000 µT) we observed, that an intermittent exposure of 5 min field-on/10 min field-off was most effective to produce DNA strand breaks in human fibroblasts. Environmental exposure to continuous ELF-EMF is rather exceptional. Different electrical household devices (hair dryer, razor, vacuum cleaner) reaching peak values up to 1 mT are often used for a short period of time (5–10 min), producing a variety of exposure

levels. To date, we could make out only one study dealing with genotoxic effects of ELF-EMF at intermittent exposure. This was done by Nordenson et al. [17], who found a significant increase of CAs in human amniotic cells (50 Hz, 30 μT, 20 s on/off). However, these results have not been corroborated by other studies as yet.

Due to the highly significant correlation between alkaline and neutral comet assays, we suggest, that predominantly non-repairable DNA DSBs are generated by ELF-EMF exposure. The observed increase in strand breaks (4.2–7.5%) after ELF-EMF exposure is quite similar to the levels found in a previous study, regarding age dependent changes in alkaline comet tailfactors in lymphocytes of healthy subjects [16] and therefore does not constitute a drastic effect. However, our data are reproducible and significant. In addition, we were able to confirm the results obtained by Lai and Singh [26], Singh and Lai [27], who performed in vivo ELF-exposure experiments (60 Hz, 0.1–0.5 mT, 2 h) and found an increase in DNA strand break levels in rat brain cells.

Moreover, due to the software controlled exposure setup, we could demonstrate a dose dependent relationship between alkaline and neutral comet assay tailfactors and applied magnetic flux density, which is unique. The guidelines of the International Commission on Non-Ionizing Radiation Protection (ICNIRP) [28] are 500 μT during workday for occupational exposures and 100 μT for 24 h per day for the general population. The on-set of genotoxic effects in our tests was at a magnetic flux density as low as 70 μT (24 h, intermittent), being well below these proposed threshold values. Moreover, the ICNIRP guidelines are dealing with continuous EMF exposure. No proposal how to handle intermittent exposures has been made as yet.

In conclusion, the outcome of this study strongly indicates a genotoxic potential of intermittent EMF. This points to the need of further studies in vivo and consideration about environmental threshold values for ELF exposure.

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