SECTION 11

Evidence for Brain Tumors (Epidemiological)
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I. INTRODUCTION

Primary central nervous system (CNS) tumors are a heterogeneous group of benign and malignant neoplasms localized in the brain, the spinal cord and their coverings. They differ in histological type, tissue of origin, anatomic site, growth pattern, age distribution, sex ratio, clinical appearance and many other features including molecular neuropathological markers. These features are not independent but little is known about the etiology of these tumors and the reason for the observed epidemiological patterns. The rapidly developing field of molecular neuropathology may provide clues to solve these problems in the future.

Annually about 57,000 new cases of CNS tumors are diagnosed in the US. The age distribution has two peaks: incidence is about 4.7 cases per 100,000 per year below 10 years of age (which is mainly due to astrocytoma of the juvenile pilocytic type, malignant glioma, medulloblastoma and tumors originating from mesodermal and embryonic tissues), and after age 15 there is a steady increase of incidence with increasing age reaching its second peak of about 68 cases per 100,000 per year at an age around 75 to 80 years (CBTRUS, 2011). The burden of CNS cancers is distinctly higher in children making up around 20% of all childhood malignancies, while in adults less than 2% of all cancers are primary brain cancers.

There are some rare cases of inherited cancer syndromes (e.g. von Hippel-Lindau disease, Li-Fraumeni syndrome) that are related to brain tumor risk, accounting for a small fraction of cases. Except for therapeutic x-rays no environmental or lifestyle factor has unequivocally been established as risk factor for brain tumors. Non-whites seem to have lower risk, and incidence tends to be higher with increasing socio-economic status. However, because of the rather advanced age of 75-80 years of peak incidence, such differences may partly be due to differences in life-expectancy. During the last decades of the 20th century some types of brain tumors show a steady increase of a few percent per year, which might to some extent be related to the introduction of computed tomography and other high-resolution neuroimaging methods. For most CNS tumors except meningioma and pituitary tumors the incidence is higher in males than females.

Since the report of Wertheimer and Leeper in 1979 of an increased incidence of brain tumors in children living in homes with an expected higher exposure to power-frequency electric and magnetic fields, exposure to electromagnetic fields have become an area of interest in the study of factors affecting brain tumor risk.

This review focuses on the radio frequency (RF) part of the electromagnetic spectrum (3 kHz to 300 GHz). However, because the epidemiology of mobile phone use is covered in another section, it will be restricted to RF exposure conditions other than microwaves from mobile phone use. Exposure to ELF magnetic fields and childhood brain tumors is covered in the chapter about childhood cancers.

II. MATERIAL AND METHODS

Published articles of relevant studies restricted to the years 1987 to 2012 were obtained by searching PubMed using the following terms:

("radio frequency" OR electromagnetic* OR microwaves) AND ("brain cancer" OR brain tumor* OR "CNS cancer" OR CNS tumor* OR glioma* OR meningioma* OR neuroma*) NOT ("power frequency" OR "low frequency") AND epidemiolog*

The search resulted in 137 hits. After removing reviews and animal or in vitro studies as well as studies of mobile phone use, 10 articles remained. A hand search in review papers (Krewski et al. 2001; Elwood 2003; Ahlbom et al. 2004; Kundi et al. 2004) and reference lists of the articles found in PubMed revealed another 9 papers; hence the final body of evidence consists of 19 studies of exposure to various types of RF fields.

Of the 19 studies 8 were cohort studies, 5 case-control studies and 6 of an ecological type. The majority of studies (11) were occupational studies, four studies investigated children, and one ecological study investigated both, adults and children.

III. EPIDEMIOLOGICAL STUDIES OF RF FIELDS AND BRAIN TUMORS

Table 10A-1 gives an overview of the 17 studies obtained by the literature search with respect to study type, assessment of exposure and outcome, confounders considered and matching variables used, number of cases included and selection method of study participants. Results are summarized in Table 10A-2.

Table 10A- 1: Synopsis of epidemiologic studies of or including brain tumors (1987 – 2007)

Study	Country/Period/Study Type	Exposure assessment	Outcome assessment	Confounders considered & matching variables(m)	Number of cases/controls or cases (cohort studies)	Selection of participants
Thomas et al. 1987	Northern New Jersey, Philadelphia, gulf coast of Lousiana/1979-1981/Case-control	Interviews with next-of-kin about occupational history – response rates: cases 74%, controls 63%; JEM (2 methods)	Death certificates verified through review of hospital records	age(m), (only males), year of death(m), area of residence(m), educational level, (lead, soldering fumes)	435/386	Cases: deaths of brain tumor or CNS tumors of white males (age>30) from death certificates Controls: deaths from other causes than brain tumors, epilepsy, etc.
Milham 1988	Washington, California/1979-1984/Cohort	Amateur radio operator license within 1/1979 to 6/1984	Mortality records	age, (only males), race, year of death	29	67829 operators, search of deaths in state registry through 1984
Selvin et al. 1992	San Francisco/1973-1988/Spatial cluster	Distance of center of census tract to microwave tower (Sutro tower)	SEER records	-	35	Search of cancer deaths of white individuals (age<21)

Study	Country/Period/Study Type	Exposure assessment	Outcome assessment	Confounders considered & matching variables(m)	Number of cases/controls or cases (cohort studies)	Selection of participants
Tynes et al. 1992	Norway/1961-1985 /Occupational cohort	Job title in 1960 and 1970 censuses and expert categorization	Cancer registry	age, (only males)	119 overall, 6 in subgroup with possible RF exposure	Cohort of 37945 male workers identified that had jobs in 1960 with possible EMF exposure. among these 3017 with possible RF exposure
Grayson 1996	US Air Force/1970-1989/Nested case-control	Detailed job history and classification based on JEM (RF/MW exposure from frequent measurements)	Screening of hospital discharge records	age(m), race(m), military rank, (ELF and ionizing radiation exposure)	230/920	Cohort of ~880000 US Air Force members with at least one completed year of service within the study period, no follow up after subjects left service
Szmigielski 1996	Poland (military)/1971 -1985/Occupational cohort	Allocation to RF/MW exposure group based on service records, documented measurements of military safety groups	Incident cases from central and regional military hospitals and military health departments	age, (only males)	~46	Annual number of ~127800 military career personnel, ~3720 RF/MW exposed per year

Study	Country/Period/Study Type	Exposure assessment	Outcome assessment	Confounders considered & matching variables(m)	Number of cases/controls or cases (cohort studies)	Selection of participants
Hocking et al. 1996	Sydney (Australia)/ 1972-1990/Ecological	Municipalities within ~4 km of 3 TV broadcasting towers considered higher exposed as compared to 6 further away	Incident and death cases from cancer registry	age, sex, calendar period	740 (incident) 606 (mortality) 64 age<15 (incident) 30 age<15 (mortality)	Study population: inner area ~135000, outer area ~450000
Tynes et al. 1996	Norway/1961-1991/ Occupational cohort	Certified radio and telegraph operators 1920-1980 (98% worked on merchant ships); spot measurements on ships with old-fashioned equipment	Cancer registry	age, (only females)	5	2619 women certified as radio or telegraph operators by Norwegian Telecom
Dolk et al. 1997a	Birmingham (GB)/ 1974-1986/Ecological	Living near a TV/FM radio transmitter (Sutton Coldfield)	Cancer registry	age, sex, calendar year, SES	332	Population (age≥15) ~408000 within 10 km of the transmitter
Dolk et al. 1997b	GB/1974-1986/	Living near a	Cancer registry	age, sex,	244	Population (age<15)

Study	Country/Period/Study Type	Exposure assessment	Outcome assessment	Confounders considered & matching variables(m)	Number of cases/controls or cases (cohort studies)	Selection of participants
	Ecological	high power (≥500 kW erp) transmitter (overall 21)		calendar year, SES		within 10 km of one of 20 high power transmitters
Lagorio et al. 1997	Italy/1962-1992/ Occupational cohort	Working as RF heat-sealer operator	Cancer deaths from registry	age, (only females), calendar period, region	1	302 women employed 1962-1992 in a plastic-ware manufacturing plant as RF sealers
Finkelstein 1998	Ontario (Canada)/ 1964-1995/ Occupational cohort	Working as a police officer (possible handheld radar exposure)	Cancer registry	age, (only males), calendar year	16	20601 male officers of Ontario Police
Morgan et al. 2000	USA/1976-1996/ Occupational cohort	Jobs classified according to work with RF emitting devices with different output power	Death certificates from states' statistics offices	age, sex, period of hire	51	All U.S. Motorola employees with at least 1 day employment 1976-1996 (195775 workers, 2,7 million person-years)

Study	Country/Period/Study Type	Exposure assessment	Outcome assessment	Confounders considered & matching variables(m)	Number of cases/controls or cases (cohort studies)	Selection of participants
Groves et al. 2002	USA/1950-1997/ Occupational cohort	6 occupational groups 3 with assumed low radar exposure (radar-, radio operator, aviation electrician's mate) and 3 with assumed high exposure (aviation electronics -, electronics -, fire control technician)	Death certificate from a state vital statistics office or National Death Index Plus	age at entry, (only males), attained age	88	40581 Navy Korean War veterans graduated 1950-54 from Navy technical schools; follow-up from graduation through 1997
Ha et al. 2003	South Korea/1993-1996/Ecological	Area <2 km around 11 high power and 31 low power AM radio transmitter and control areas >2 km from any transmitter	Cancer cases from insurance records	age, sex (direct and indirect standardization)	45/not specified	Census and residents registration data 1995 (population size between 3152 and 126523 at the different sites)
Park et al. 2004	South Korea/1994-1995/Ecological	10 areas with a AM radio transmitter ≥100kW	Cancer deaths from death certificates	age, sex (direct standardization)	30/100	Census data from 1990

Study	Country/Period/Study Type	Exposure assessment	Outcome assessment	Confounders considered & matching variables(m)	Number of cases/controls or cases (cohort studies)	Selection of participants
Berg et al. 2006	Germany/2000-2003/ Case-control	JEM from occupational history collected in interview	Histological verified cases of glioma and meningioma	age(m), sex(m), region(m), SES, urban/rural, smoking, ionizing rad. exposure	Glioma 366/732 Meningioma 381/762	All histological confirmed cases of glioma and meningioma from 4 neurosurgical clinics (age: 30-69) (part.rate 84%); frequency matched controls from population registry (part.rate 63%)
Schüz et al. 2006	Germany/2000-2003/ Case-control	Questionnaire about DECT cordless phone base station near the bed	Histological verified cases of glioma and meningioma	age(m), sex(m), region(m), SES, urban/rural, smoking, ionizing rad. exposure	Glioma 366/732 Meningioma 381/762	All histological confirmed cases of glioma and meningioma from 4 neurosurgical clinics (age: 30-69) (part.rate 84%); frequency matched controls from population registry (part.rate 63%)
Ha et al. 2007	South Korea/1993-1999/Case-control	Distance from 31 AM radio transmitters and 49 radio antennas, measurements and calculation of	Cases of brain cancer from verified by entry into cancer registry	age(m), sex(m), year of diagnosis(m), SES, population density	956/1020	All cases of brain cancer (age<15) from 14 hospitals and matched hospital controls with respiratory diseases

Study	Country/Period/Study Type	Exposure assessment	Outcome assessment	Confounders considered & matching variables(m)	Number of cases/controls or cases (cohort studies)	Selection of participants
		total RF electric field strength				

SES…socio-economic status, JEM…job exposure matrix, erp…equivalent radiation power, RF/MW…radio frequency/microwaves, CNS…central nervous system, ELF…extremely low frequency

Table 10A- 2: Synopsis of main results of brain tumor studies (1987 – 2007)

Study	Endpoint	Exposure category	Meas.	Outcome [95% CI]
Thomas et al. 1987	Brain tumor deaths (ICD not specified)	Ever exposed to RF	OR	1.6 [1.0 – 2.4]
		Electrical/electronics job	OR	2.3 [1.3 – 4.2]
		Unexposed*		
		Ever exposed < 5 y	OR	1.0
		5-19 y	OR	2.3
		20+ y	OR	2.0
Milham 1988	Brain cancer deaths (ICD-8: 191)	All	SMR	1.39 [0.93 – 2.00]
		Novice[a]	SMR	0.34
		Technician	SMR	1.12
		General	SMR	1.75
		Advanced	SMR	1.74
		Extra	SMR	1.14
Selvin et al. 1992	Brain cancer deaths (ICD-O: 191.2)	> 3.5 km distance from tower*		
		≤ 3.5 km[b]	RR	1.16 [0.60 – 2.26]
Tynes et al. 1992	Incident brain cancer (ICD-7: 193)	All with possible EMF exposure	SIR	1.09 [0.90 – 1.41]
		Subgroup possible RF exposure[c]	SIR	0.49 [0.18 – 1.06]
Grayson 1996	Incident brain cancer (ICD-9: 191)	Never RF/MW exposed*		
		Ever exposed	OR	1.39 [1.01 – 1.90]
Szmigielski 1996	Incident nervous system & brain tumors	RF/MW exposed	OER	1.91 [1.08 – 3.47]
Hocking et al. 1996	Brain cancer (ICD-9: 191)	Outer area*		
		Inner area (incident, overall)	RR	0.89 [0.71 – 1.11]
		Inner area (mortality, overall)	RR	0.82 [0.63 – 1.07]
		Inner area (incident, age<15)	RR	1.10 [0.59 – 2.06]
		Inner area (mortality, age<15)	RR	0.73 [0.26 – 2.10]
Tynes et al. 1996	Incident brain cancer (ICD-7: 193)	All	SIR	1.0 [0.3 – 2.3]
Dolk et al. 1997a	Incident brain tumors (ICD-8/9: 191, 192)	0-2 km from transmitter	OER	1.29 [0.80 – 2.06]
		0-10 km from transmitter	OER	1.04 [0.94 – 1.16]
Dolk et al. 1997b	Incident brain tumors (ICD-8/9: 191, 192)	0-2 km from transmitter	OER	0.62 [0.17 – 1.59]
		0-10 km from transmitter	OER	1.06 [0.93 – 1.20]

Study	Endpoint	Exposure category	Meas.	Outcome [95% CI]
Lagorio et al. 1997	Brain cancer deaths (ICD-9: 191)	RF sealer operator	OER	1 : 0.1
Finkelstein 1998	Incident brain cancer (ICD-9: 191)	All police officers	SIR	0.84 [0.48 – 1.36]
Morgan et al. 2000	Incident brain cancer (ICD-9: 191)	No RF exposure*		
		Low[d]	RR	0.92 [0.43 – 1.77]
		Moderate	RR	1.18 [0.36 – 2.92]
		High	RR	1.07 [0.32 – 2.66]
Groves et al. 2002	Brain cancer deaths (ICD-9: 191)	Low radar exposure*		
		High radar exposure	RR	0.65 [0.43 – 1.01]
Ha et al. 2003	Brain cancer (ICD-10:C70-C72)	Low power transmitters*		
		High power transmitters	SIR	1.8 [0.8 – 11.1]
		Control sites (>2 km)*		
		100 kW transmitter	OER	2.27 [1.30 – 3.67]
		250 kW	OER	0.86 [0.41 – 1.59]
		500 kW	OER	1.47 [0.84 – 2.38]
		1500 kW	OER	2.19 [0.45 – 6.39]
Park et al. 2004	Brain cancer deaths (ICD-10:C69-C72)	Control area*		
		≥100 kW transmitter	SMR	1.52 [0.61 – 3.75]
Berg et al. 2006	Incident glioma (ICD-O3: C71)	No occup. RF/MW exposure*		
		Probably no exposure	OR	0.84 [0.48 – 1.46]
		Probable exposure	OR	0.84 [0.46 – 1.56]
		High exposure	OR	1.22 [0.69 – 2.15]
		No high exposure*		
		High exposure <10 y	OR	1.11 [0.48 – 2.56]
		High exposure ≥ 10 y	OR	1.39 [0.67 – 2.88]
	Incident meningioma (ICD-O3: C70.0)	No occup. RF/MW exposure*		
		Probably no exposure	OR	1.11 [0.57 – 2.15]
		Probable exposure	OR	1.01 [0.52 – 1.93]
		High exposure	OR	1.34 [0.61 – 2.96]
		No high exposure*		
		High exposure <10 y	OR	1.15 [0.37 – 3.48]

Study	Endpoint	Exposure category	Meas.	Outcome [95% CI]
		High exposure ≥ 10 y	OR	1.55 [0.52 – 4.62]
Schüz et al. 2006	Incident glioma (ICD-O3: C71)	DECT near bed	OR	0.82 [0.29 – 2.33]
	Incident meningioma (ICD-O3: C70.0)	DECT near bed	OR	0.83 [0.29 – 2.36]
Ha et al. 2007	All brain cancers (ICD-10: C70-C72)	≤2 km	OR	1.42 [0.38 – 5.28]
		2-4 km	OR	1.40 [0.77 – 2.56]
		4-6 km	OR	1.02 [0.66 – 1.57]
		6-8 km	OR	1.08 [0.73 – 1.59]
		8-10 km	OR	0.94 [0.67 – 1.33]
		10-20 km	OR	1.01 [0.77 – 1.34]
		>20 km*		

* Reference
[a] From Milham 1988b, license classes as proxy for exposure duration
[b] Based on the assumption that exposure is higher near the microwave tower
[c] Computed based on Table 5 in Tynes et al. 1992
[d] Classification according to power output of equipment used for longest period of employment

OR…odds-ratio, SIR…standardized incidence ratio, SMR…standardized mortality ratio, RR…relative risk (rate ratio), OER…observed/expected ratio

In the following paragraphs each study is briefly discussed with respect to its strengths and weaknesses.

A. Thomas et al. 1987

This case-control study included 435 deaths from brain or CNS tumors and 386 deaths from other causes as controls. Only adult males were included. Basis of data collection on occupational history were interviews with next-of-kin. Two methods of classification were used: one method assigned subjects to one of three categories (never exposed to RF/ever exposed to RF in an electrical or electronics job/ever exposed to RF but not in an electrical or electronics job), the other method consisted of a classification of each job by an industrial hygienist for presumed exposure to RF, soldering fumes, and lead. Both methods revealed significantly increased brain tumor risks of presumed occupational exposure to RF fields. This increase was due to an association in electronics and electrical jobs with astrocytic tumors as the predominant outcome associated with employment in these categories. In addition a significant increase of brain tumor risk was found for increasing duration of exposure.

Although relying on information of next-of-kin could be a source of misclassification, one strength of this study is it's relying on occupational history only that could be assumed to be more accurate than recall of exposure to various agents. The two methods of classification led to almost the same results, which lends support to the hypothesis that indeed exposure in electrical and electronics jobs is associated with an increased brain tumor risk. Due to the relationship between RF exposure and exposure to lead, solvents or soldering fumes in these jobs, it is not possible to separate effects of these exposures. Soldering fumes were never investigates with respect to brain tumors, and the hypothesis of an association with sinonasal cancer could not be corroborated so far. However, analysis of exposure to lead did not show a consistent relationship with brain tumor risk, indicating that it may not confound the relationship to RF exposure.

Because this study is of dead cases only it is likely over-representing high grade brain tumors that may not all be associated with exposure leading to an effect dilution. Exposure misclassification, if it is non-differential in cases and controls, also reduces effect estimates.

A weakness of this study is obviously its lack of an exposure indicator other than the occupational category. While there is no doubt that in these jobs some exposure to RF fields occur quite regularly, specific characteristics including frequency ranges, modulation, intensity, duration and distance from the source vary considerably. Overall the study (as well as two earlier ones outside the search window: Lin et al. 1985 and Milham 1985) are sufficient to formulate a research hypothesis that can be tested in appropriately designed subsequent investigations. Unfortunately such studies have never been conducted.

B. Milham 1988

In this cohort study of 67,829 amateur radio operators holding a license within 1/1979 to 6/1984 in Washington and California 29 brain tumor deaths occurred during the follow up period with 21 expected.

It should be noted that there was a substantial and statistically significant lower number of overall deaths of less than three quarters of deaths expected from country mortality rates. This could be due to both a 'healthy-worker' effect as well as an effect of socio-economic status. In lieu of computing standardized mortality ratios (SMR) it may be instructive to look at the proportional mortality rates in the reference population and the amateur radio operators: 0.6% of all deaths are expected to be due to brain tumors in the reference population while in amateur radio operators twice as many occurred (1.2%). Whether or not this is an indication of an increased brain tumor risk due to RF exposure is difficult to assess. First of all, this study is a register only investigation and no information on intensity, frequency and duration of engagement in amateur radio operations were available. In a later analysis the author reported about results using a proxy of intensity and duration of exposure: the license class. In this analysis indications of an increase of risk with increasing license class were obtained.

This study could and should have started off a thorough follow up of amateur radio operators and nested case-control studies to address the problem of potential confounders and to narrow down the conditions that may be responsible for the increased mortality from some cancers. It is another loose end that leaves us without a clear message.

Although no risk factor for brain cancer except therapeutic ionizing radiation is known, there are some indications that risk increases with social class. The reason for this association is unknown but life-style factors may play a role as well as concomitant causes of death that

could lead to a spurious reduction of risk in lower class populations because brain tumors have their peak close to life-expectancy.

C. Selvin et al. 1992

The objective of this investigation was not primarily to study the relationship between RF exposure and childhood cancer but to address the general problem of how to assess disease incidence or mortality in relation to a point source. As the point source the Sutro Tower in San Francisco, the only microwaves emitting tower in this county, was chosen. A total of 35 brain tumor deaths occurred among 50,686 white individuals at risk aged less than 21 in the years 1973-88 in an area of approximately 6 km around the tower. The exact location of residence could not be obtained; therefore each case was located in the center of the census tract. Different methods of analysis were applied to assess a potential relationship between distance from the tower and brain tumor risk. Relative risk for brain tumors for a distance less than 3.5 km from Sutro Tower compared to more than 3.5 km was 1.162 and not significant.

The study explored different methodological procedures and has its merits from a methodological point of view. However, it starts from the wrong assumption: that distance to a point source is a valid proxy for intensity of exposure. Under ideal conditions of spherical symmetry of an emission this assumption holds, however, there are almost no real life situations where this assumption is sufficiently close to actual exposure levels. And it is definitely not true for the Sutro Tower. Radiations from the antennae are directed towards the horizon and the complex pattern of emission with main and side lobes results in a complex pattern of RF exposure at ground level. Furthermore, the area is topographically structured with hills and valleys such that areas of high exposure at the vertices are in close proximity to areas of low exposure at the shadowed side downhill.

Studying the relationship between a point source and disease is not only difficult due to the complex relationship between distance and exposure but also because of the fact that humans are not stable at a certain location. This is of greater importance for adults who may commute from and to work places and have generally a greater radius of activity as compared to children. Nevertheless, there is at least a high chance of one long-lasting stable location that is when people sleep in their beds. Therefore, studies in relation to a point source should attempt to assess exposure at the location of the bed. Because the objective of this study was not the

assessment of a potential brain tumor risk but the application of methods for the analysis of spatial data, no attempts were made to measure actual exposure.

D. Tynes et al. 1992

In this study information on occupations obtained for all Norwegians every 10 years was used to assess cancer incidence in relation to job titles. In 1960 37,945 male workers were identified that had jobs with possible exposure to EMFs and among these 3,017 with possible RF exposure. Overall 119 brain tumor cases were found in the cancer registry between 1961 and 1985. Of these cases 6 occurred in the subgroup of workers possibly exposed to RF fields. The overall expected number of brain tumor cases was 109 and 12 for the subgroup with possible RF exposure. Hence no increased brain tumor risk could be detected.

Despite the long follow-up period of 25 years with an accumulated number of 65,500 person-years the expected number of brain tumors diagnosed during that period is too low to detect a moderately elevated risk of 1.3 to 1.5. Furthermore, the follow up period just reaches the median induction period for brain tumors as delineated from studies on ionizing radiation.

As mentioned above, all studies solely relying on job titles lead to exposure misclassification and, therefore, to a dilution of risk. For dichotomous exposure variables (exposed/not exposed) and assuming a negligibly small proportion of exposed in the reference population standardized incidence ratios (SIR) are biased by a factor (1+f*(SIR-1))/SIR, if f denotes the fraction of true exposed and SIR is the true incidence ratio. Hence a true SIR of 2.0 is reduced to 1.5 if only 50% in the cohort are actually exposed. The observed SIR is further reduced if the assumption of a negligible fraction of exposed in the reference population is wrong. In this case the bias factor given above is further divided by (1+g*(SIR-1)), where g is the fraction of exposed in the general population.

While a cohort study that is based on registry data has the advantage of independence from recall errors and selection bias due to possible differential participation, it has the disadvantage that registry data are generally insufficient to provide reliable exposure indicators. While no association with brain tumors could be detected in this study it revealed an increased number of leukemia cases in occupations with possible RF exposure. This could

be due to the higher incidence of leukemia or to a stronger association or to the shorter latency and various other reasons including chance.

E. Grayson 1996

In this case-control study nested within approx. 880,000 US Air Force personnel with at least one years of service during the study period of 1970-89, primary malignant brain tumor cases were ascertained by screening hospital discharge records. The study included only males and only as long as they were on Air Force records. From 246 cases detected 16 were dropped due to incomplete or ambiguous data. For each case four controls were randomly selected from the case's risk set matching it exactly on year of birth and race. Controls that were diagnosed with diseases possibly associated with EMF exposure (leukemia, breast cancer, malignant melanoma) were excluded from the risk set.

A strength of this study is the detailed job history filed for each cohort member that could be used for retrospective exposure assessment. Furthermore, Air Force files contained detailed data from personal dosímetry on ionizing radiation for the different posts and jobs. Classification of RF field exposure was based on a detailed job exposure matrix with over 1,950 entries, indexing 552 different job titles. One source of classification was recorded events of exposure to RF fields above 100 W/m^2. By this method probable exposure was assigned if for a job such events were recorded in the past as well as for closely related jobs. Possible exposure was assigned for jobs that required operation of RF emitters but without recorded overexposure.

A further strength is the thorough consideration of possible confounders. Because of the possible relationship of brain tumor risk with socio-economic status (SES), military rank was used as a surrogate for SES and included in the analysis as well as ionizing radiation exposure that has previously been shown to increase brain tumor risk.

Exposure to RF fields was associated with a moderate but statistically significant increased risk of OR=1.39. Investigation of duration of exposure was compromised by an ambiguity introduced due to the calculation of an exposure score as the product of exposure and months. Nevertheless, for those ever exposed there were indications of an increasing risk with increasing exposure duration.

A weakness of this investigation is its incomplete follow-up of cohort members. This could have resulted in an underestimation of the true risk. Leaving the Air Force could have been more likely in those exposed to RF fields and developing a brain tumor. Some malignant brain tumors have early signs that could be incompatible with the Air Force job especially if involving operation of RF equipment (like seizures, severe headaches, somnolence, and absences). Because the study did not involve personal contact it is free of other selection biases.

F. Szmigielski 1996

In this military cohort study of cancer morbidity Polish military career personnel was assessed for occupational exposure to RF fields based on service records. The study covered 15 years (1971-85) including approx. 128,000 persons per year. Expected rates for 12 cancer types were calculated based on the age specific morbidity in those classified as unexposed.

For brain and nervous system tumors a significantly increased ratio of observed to expected (OER=1.91) was found. Other malignancies with significantly increased incidence in exposed were: esophageal and stomach cancers, colorectal cancers, melanoma, and leukemia/lymphoma.

A strength of this study is its substantial size with almost 2 million person-years of follow-up. Furthermore, accurate military records on job assignment and on exposure from military safety groups gives a unique opportunity to assess long-term exposure effects based on already filed data.

Some important data are missing because they were military classified information that could not be provided in the paper. This includes the exact number of cases of the different neoplasms. However, from the data presented an observed number of brain tumors of about 46 can be calculated.

The study has been criticized for an alleged bias because more information on risk factors was available for cancer cases. It is true that military medical boards collected data for cases such as life style factors and exposure to possible carcinogens during service, however, at no stage this information entered the analysis. Therefore, this criticism is unfounded. Such information could have been utilized within a nested case-control study applying the same methods of assessment of risk factors for controls as has been done for cases. Because some findings,

such as the increased risk for esophagus/stomach cancer, that are rarely reported in relation to RF exposure warrant further study, such a nested case-control approach is recommended. It could, albeit with some difficulties, even be successfully conducted retrospectively.

G. Hocking et al. 1996

In an ecological study cancer incidence and mortality in nine municipalities of northern Sydney during 1972-90 three of which surround three TV towers were assessed. Population size in the three municipalities located within a radius of approx. 4 km around the TV towers amounts to 135,000, while population size in the six municipalities further away was 450,000. High-power transmission commenced in 1956, an additional 100 kW transmission started in 1965 and another 300 kV broadcast in 1980. Carrier frequencies varied between 63 and 533 MHz for TV broadcasting and were around 100 MHz for FM radio broadcast.

During the study period 740 primary malignant brain tumors were diagnosed in adults and 64 in children, 606 deaths due to brain cancer occurred in adults and 30 in children. While incidence of lymphatic leukemia was significantly higher in adults as well as in children inhabiting the three municipalities surrounding the transmission towers compared to the six districts further away, brain tumor incidence was not significantly elevated (RR=0.89 in adults and 1.10 in children).

As has been stated above, distance from a transmitter is a poor proxy for exposure. Some measurements done in the study area obtained levels much lower than those calculated from the power emitted and antenna gain. Several factors are responsible for this effect: multiple reflections, attenuation by buildings and vegetation, ground undulations, non-coincidence of maxima for the different signals as well as complex radiation characteristics of the broadcast antennae.

The exact location of the residence of cases could not be provided which reduces the potential of the study to relate incidences to measurements or calculations of RF fields. Authors discussed some potential sources of bias such as migration and other exposures in the different regions. However, the most important disadvantage in such studies is that individual risk factors cannot be adjusted for. Both spurious positive as well as false negative results can be obtained by disregarding such individual variables.

H. Tynes et al. 1996

In a historical cohort study 2,619 Norwegian female radio and telegraph operators certified between 1920 and 1980 were followed from 1961 through 1991 for entries in the cancer registry. During this period a total of 140 cases of cancer occurred which are about 20% more than expected from the Norwegian population. Among these were 5 brain tumor cases closely matching the number expected.

An excess for breast cancer was found in this study that may be related to a combination of RF field exposure and night work. For other cancers including brain cancer numbers of cases were too low to address exposure risk.

In this very thoroughly conducted study including a nested case-control approach for breast cancer, measurements at historical transmitters on ships, comparison with women at other jobs on sea, brain tumors were not distinctly higher than expected from the reference population. However, because of the limited cohort size a moderately increased risk cannot be excluded.

I. Dolk et al. 1997a

This ecological small area study of cancer incidence 1974-86 near the Sutton Coldfield TV/radio transmitter at the northern edge of the city of Birmingham (England) was initiated by an unconfirmed report of a ‘cluster’ of leukemias and lymphomas. The transmitter came into service in 1949. Transmission at 1 megawatt (effective radiated power erp) began in 1964, at 3 MW in 1969, and at 4 MW in 1982. The tower has a height of 240 m with no big hills in the surrounding area. The study area was defined by a circle of 10 km radius centered at the transmitter. The population within this area was about 408,000. All cancers, excluding non-melanoma skin cancer, were considered focusing on hematopoietic and lymphatic cancers, brain and nervous system cancers, eye cancer, and male breast cancer. Childhood cancers were restricted to all cancers and all leukemias.

In the study area a small but significant excess of all cancers was observed in adults. All leukemias and non-Hodgkin’s lymphoma were particularly elevated and incidence within 2 to 4 km from the tower was about 30% higher than expected. Brain tumors were only analyzed for distances of within 2 km and the whole study area. Within 2 km an increased OER of 1.29

for all brain tumors and 1.31 for malignant brain tumors was calculated based on 17 and 12 cases, respectively.

Also this investigation suffers from using distance from the tower as proxy for intensity of exposure. The wrong assumption that exposure decreases with increasing distance invalidates the statistical trend test applied. Measurements conducted in the study area revealed the poor relationship with distance but without consequences on the evaluation of the data. Overall the study is consistent with a moderately increased risk of hematopoietic and lymphatic cancers as well as some other cancers including brain cancer in the vicinity of high-power transmitters that, if related to RF fields, must be substantially higher for actual exposure.

The Sutton Coldfield study was later continued (Cooper & Saunders 2001) to cover the period 1987-94. The study revealed, compared to the earlier period, an almost unchanged increase of leukemias and non-Hodgkin's lymphoma in adults and a slight increase in children.

J. Dolk et al. 1997b

Because the Sutton Coldfield study was triggered by a cluster report and to provide independent test of hypotheses arising from that study, similar methods as applied in the previous study were used to study all high-power TV/radio transmitters (≥ 500 kW ERP) in Great Britain. In adults leukemias, bladder cancer, and skin melanoma, and in children, leukemias and brain tumors were studied. The study period was 1974-86 for England and somewhat shorter in Wales and Scotland.

Although population density around transmitters was not always as high as in the case of the Sutton Coldfield tower, with an average population density of only about one third of that around Sutton Coldfield tower within 2 km from the towers, in the most important range of 2 to 4 km from the transmitters, where in many cases the maximum of radiated RF at ground level is reached, population density was similar. The study of all high-power transmitters essentially corroborated the findings for adult leukemias with an increase of incidence between 10 and 50% in the distance band of 2 to 4 km from the transmitters for the different transmitter types. Most of these increased incidences were statistically significant.

For children only the incidence in the whole study area and within a distance of 2 km was calculated, which is unfortunate because the area close to the towers is sparsely populated and

exposure is low. Number of brain tumors in children was slightly above expectation (244 observed and 231 expected).

In contrast to the interpretation by the authors, the study of all high power transmitters essentially replicated and supported the findings of an excess incidence of leukemias in relation to RF emission from TV/radio towers. Because the different heights and radiation characteristics of the transmitters result in different exposure patterns at ground level, the consistent increase in an area that is likely close to the maximum of exposure supports the hypothesis of an association.

K. Lagorio et al. 1997

A mortality study of a cohort of 481 female plastic-ware workers employed between 1962 and 1992 in an Italian plant, 302 of which were engaged in the sealing department with exposure to RF fields, was reported by Lagorio et al. (1997). For RF-sealers 6,772 person-years of follow-up were accumulated and overall 9 deaths occurred, 6 of which were from malignant neoplasms (which are twice as many as expected from comparison with the local reference population). In the 31 years only one brain cancer occurred but only 0.1 were expected.

Although the small size of the cohort and the potential exposure to other agents except RF fields such as solvents and vinyl chloride prohibit far reaching conclusion, much more of such thorough follow-up studies of exposed cohorts are needed to accumulate a body of evidence that can provide a useful basis for analysis.

L. Finkelstein 1998

A preliminary study intended to form the basis for an assessment of cancer risks associated with handheld radar devices was conducted among a cohort of 20,601 male Ontario police officers. The retrospective follow up covered the period of 1964-95. By linkage with the cancer registry and mortality database 650 cases of cancer were detected.

Testicular cancer and melanoma showed an excess incidence while overall cancer incidence was reduced as expected from a working cohort. Overall 16 cases of primary malignant brain tumors occurred which is slightly less than expected.

The author had difficulties to build up a proper cohort because some departments refused to participate and others couldn't spare the time to provide lists of all officers employed during the target period. Furthermore, while cancer sites of primary interest showed actually an increased incidence calling for a nested case-control approach, this study was never conducted due to lack of interest and support of the authorities.

M. Morgan et al. 2000

In an occupational cohort study all US Motorola employees with at least 6 months cumulative employment and at least 1 day of employment in the period 1976-96 were included. A total of 195,775 workers contributing about 2.7 million person-years were available for the study. The cohort was compared to the SSA Master Mortality File and the National Death Index to obtain vital status. Death certificates were obtained by states' vital statistics offices and company records. Exposure was assessed by expert opinion. Four RF exposure groups were defined with increasing level of estimated RF exposure. Only about 5% of the total cohort was classified as highly exposed and more than 70% with only background exposure. Neither private nor occupational mobile phone use was included.

Overall 6,296 deaths occurred in the cohort in 21 years, which were only two thirds of deaths expected from mortality data of the four countries where most Motorola facilities are located. This reduction is too pronounced to be solely due to a healthy worker effect, other factors such as higher SES must have contributed, an interpretation supported by the substantial reduction of mortality from all life-style associated causes of death. Internal comparisons were done for mortality from brain cancer and hematopoietic and lymphatic cancers. Brain tumor mortality was slightly but insignificantly elevated in high and moderately high exposed workers as compared to those with no or low RF exposure.

This study of a huge cohort demonstrates the limitations of such a study design. The majority of the cohort (58%) consisted of retired or terminated workers that may or may not have accumulated further RF exposure at other companies. Furthermore, it can be assumed that Motorola employees were among the first that used mobile phones at the workplace and

privately. Neglecting mobile phone use may diminish the gradient of exposures between occupational groups studied. It would have been better to conduct nested case-control studies instead of using internal comparison that may be compromised by mobility bias, exposure misclassification and use of mobile phones.

N. Groves et al. 2002

In this military cohort study of 40,581 men followed from the year of graduation (1950-1954) from Navy technical schools through 1997, known as the Korean War Veterans study, groups of sailors with imputed difference in likelihood and amount of exposure to radar waves were compared with respect to mortality. The original study, with a follow up through 1974, (Robinette et al. 1980) reported increased risks of cancer of the hematopoietic and lymphatic system, of the lung and digestive system for the high exposure group but was handicapped by the lack of information on date of birth of the cohort members. For the extended follow up study many missing birth dates were found in the Veterans Administration Master Index. Nevertheless, birth date remained unknown for over 8% of the cohort. Based on expert opinion low RF exposure was assigned to job classifications of radioman, radarman, and aviation electrician's mate, high exposure stratum included men with job classifications of electronics technician, aviation electronics technician, and fire control technician.

By matching against the Social Security Administration's Death Master File and the National Death Index 8,393 deceased subjects were identified through 1997. This number is substantially and significantly lower as expected from the male white US population. A healthy soldier effect may have been responsible for a lower mortality rate in the 1950ies but cannot explain the reduced mortality after 40 years. It has not been reported how long the cohort members stayed in service nor were life-style factors investigated; however, of more than 40% of the cohort no social security number could be obtained suggesting possible under-estimation of deaths.

Comparison of high- with low-exposure groups revealed significantly lower mortality from life-style associated causes of death (lung cancer, vascular diseases, diabetes mellitus, chronic obstructive pulmonary disease, and liver cirrhosis) and significantly higher mortality from all leukemias and external causes of death. Increased mortality from leukemias was found in all high exposure groups but the most pronounced increase was observed in aviation electronics

technicians. Brain cancer was less frequent in all high exposure groups compared to the low exposure category.

The long period of follow up of this large cohort with start of follow up almost at the same time (1950-54) and at a time when exposure commenced is a great advantage of this investigation. However, there are a number of shortcomings: follow up was possibly incomplete by unknown social security number of a substantial proportion of the cohort; almost half of all deaths in the first 20 years were from external causes which could have obscured an effect of exposure; duration and intensity of exposure is unknown as well as potential exposure after leaving the Navy; classification into low and high exposure groups may introduce substantial misclassification. In the earlier report, inspection of Navy records for a sample from the high exposure group revealed that 24% had no exposure to radar waves at all.

Concerning brain tumors, assuming an effect of radar exposure on tumor growth rate, exposure during the Korean War and no exposure afterwards would be expected to result in only a slightly increased risk during a period of about 10 years after the war. Sailors were about 20 to 25 years at that time. The fraction with an already initiated brain tumor during this age range is estimated to be less than 3 in 100,000 per year. Increase of growth rate even if substantial cannot result in an effect observable in a cohort of that size. If radar exposure increases the likelihood of malignant transformation this could increase the incidence during a time window of 10 to 30 years after the exposure period. Results of the Israeli study of x-ray treated tinea capitis (Sadetzki et al. 2005) suggests an average latency of about 20-25 years, however, risk decreased with increasing age at first exposure to x-rays. Taking the data on ionizing radiation as a guiding principle for brain tumor initiation, radar exposure of sailors during their twenties might result in an increase of brain tumor mortality of about 10 to 15%, i.e. a maximum of 8 additional cases among 20,000. Considering the biases of the study such a low risk is easily obscured. Hence neither tumor promotion nor initiation may be detected in this study even if there is an increased risk. Because of the mentioned limitation to a certain time window with possibly increased incidence due to exposures during service in the Korean War, it would have been instructive to compute Kaplan-Meier estimates for cumulative brain tumor mortality.

O. Ha et al. 2002

An ecological study around 11 high-power AM transmitter study sites (i.e., 100–1,500-kW transmission power) and 31 low-power study sites (i.e., 50-kW transmission power) used for comparison was conducted in South Korea. For each high-power site four control areas located in the same or nearest adjacent province as the high-power site, but were at least 2 km from any of the transmitters were chosen. The incidence of cancer within a 2-km radius of each transmitter and within control districts was obtained from Korean medical-insurance records for the years 1993 through 1996. Standardized incidence ratios (SIR) of high- against low-power transmitter areas were reported and additionally observed-to-expected ratios for each type of transmitter. SIRs were elevated for all cancers and for female brain cancer. Concerning transmitter types, for all types except 250 kW elevated OER for brain cancer were obtained (statistically significant for 100 kW).

Due to the complex relationship between distance and field strength, depending on antenna type and characteristics, height above ground level, orographic conditions, electrical properties of the terrain, etc., choice of a 2-km radius for all transmitters might not have been the best option to select the highest exposure group.

P. Park et al. 2004

A similar design as in the study of Ha et al. (2003) was applied in this ecological investigation of cancer deaths. Ten high-power (i.e., 100–1,500-kW transmission power) sites were chosen and compared to four control districts as in the previous study. Standardized mortality ratios were elevated for all single cancer sites but significant only for total cancer deaths. For brain cancer the ratio was 1.52 and statistically not significant.

The same criticism as for the study of Ha et al. (2003) applies to this study. Both studies share the limitations inherent in the ecological study design.

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Q. Berg et al. 2006

In the German part of the Interphone study special attention was paid to occupational history and exposure to RF fields at workplaces. Incident meningioma (n=381, response rate 88%) and glioma cases (n=366, response rate 80%) aged 30-69 years were selected from four

neurological clinics. Overall 1,535 (participation rate 63%) were randomly selected from population registries matched to the cases by sex, age, and region. Most cases were interviewed during their stay in hospitals, controls were interviewed at home. The interview contained several screening questions about occupations that are probably associated with RF exposure. If any of these screening questions were marked additional questions were asked about the job. Based on the literature and the evaluation by two industrial hygienists a classification into the following categories was performed: no RF exposure/not probably RF exposed/probably RF exposed/highly RF exposed. In total about 13% (299 cases and controls) were classified with at least possible RF exposure at the workplace. Analyses were adjusted for region, sex, age, SES, urban/rural residence, ionizing radiation exposure in the head/neck region. Mobile phone use was not considered as a confounder.

While overall RF exposure at workplaces showed no increased odds-ratios, high exposure and especially for durations of 10 years or more resulted in elevated risk estimates that were, however, not significant. This result was similar for meningioma (OR=1.55 for high exposure for 10 years or more) and glioma (OR=1.39).

The study tried to assess potential workplace exposure as precisely as possible in a personal interview, but still misclassification may have occurred especially in the probable and not probable categories while the high exposure group is likely to have had at least occasionally above average RF exposure. Odds ratios are in the range expected if exposure results in a substantial increase of growth rate. The small number of highly and long-term exposed cases (13 glioma and 6 meningioma) prohibit, however, far reaching conclusions.

R. Schüz et al. 2006

In the same study as mentioned above also exposure to emissions from DECT (Digital Enhanced Cordless Telecommunications) base stations near the bed were analyzed. Both, for glioma and meningioma, not significantly decreased odds ratio were reported. There was also no increasing risk observed with duration of exposure to DECT cordless phone base stations. The study was limited due to the small number of exposed subjects and the short exposure duration. It is unlikely that after these short exposures periods an increased risk can be observed.

S. Hu et al. 2007

The study from South Korea that was a major improvement in investigating the possible association between RF EMF exposure and cancer risk applied not only instead of an ecological approach the case-control paradigm but also used an interesting method to estimate individual exposure. This method seems a reasonable compromise between effort and precision. The study included leukemia and brain cancer patients under age 15 years and controls with respiratory illnesses matched to cases on age, sex, and year of diagnosis (1993–1999). All were selected from 14 South Korean hospitals using the South Korean Medical Insurance Data System. Residential addresses were obtained from medical records so that no direct contact with the participants was necessary. Authors developed an exposure prediction program incorporating a geographic information system that was modified by the results of actual measurements carried out systematically at defined locations and during driving along specific trajectories. Furthermore, electrical characteristics of the environment were considered. This method was used to estimate RF EMF exposure from 31 AM radio transmitters with a power of 20 kW or more. A total of 1,928 leukemia patients, 956 brain cancer patients, and 3,082 controls were included.

A significantly increased odds ratio was obtained for childhood leukemia at a distance of 2 km or less from the transmitters relative to a distance of >20 km. In response to a critical comment by Schüz et al. (2008) authors recalculated the risk estimates for total and peak RF EMF exposure (Hu et al. 2008) and reported for the highest quartile of peak RF EMF exposure a significantly increased risk of ALL. For childhood brain cancers insignificantly increased risks of about 1.4 for ≤2 km and 2-4 km from the transmitter were obtained.

It seems that there were problems with the RF EMF estimates since peak and total field strengths had quite different results and also the correlation with peak exposure and distance was much higher than with total exposure suggesting that more distant transmitters led to a decrease in the gradient of exposures. The measurements are not reported for the different transmitter types and therefore it is difficult to assess their validity. For very high power transmitters (1,500 kW) the relationship is known to be not monotonous which cannot be discriminated in the figure shown in the article. Overall the study has an improved methodology due to the case-control and registry approach. However, the methods to assess actual exposure need to be further improved.

IV. EVALUATION OF THE EVIDENCE

Due to the varying endpoints, methods used and populations included the meta-analysis shown in fig.1 applied the random effects model and DerSimonian-Laird estimate of the overall risk and confidence interval. Only few studies found clear indications of an association between RF exposure and brain tumors: one cohort study (Szmigielski 1996) and two case-control studies (Thomas et al. 1987, Grayson 1996). None of the ecological studies except for Ha et al. (2003) for one of the AM transmitter types demonstrated a significantly increased risk in the vicinity of RF antennas.

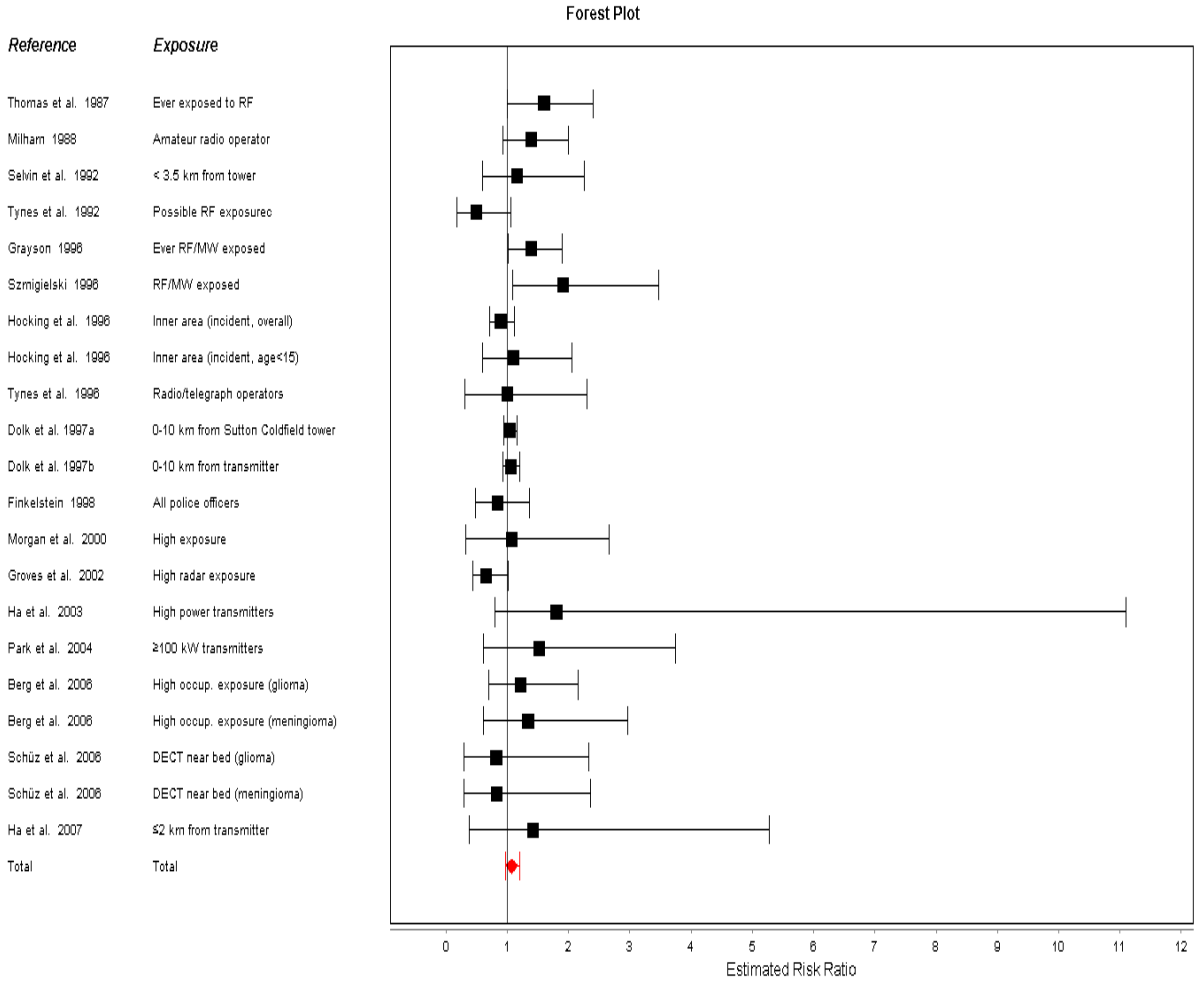

Fig. 1: Forest plot of risk estimates for RF exposure with respect to brain tumors and DerSimonian-Laird overall estimate

The meta-analytical estimate of the risk was 1.08 (95% confidence interval: 0.97 – 1.20). The discussion of the 19 published investigations revealed shortcomings in all studies. The

greatest problem was encountered in the difficulties to reliably assess actual exposure. Even if we don't know the relevant aspect of the exposure, if any, that is responsible for an increased risk, the type, duration and amount of exposure must be determined in order to use the studies in derivations of exposure standards. None of the studies included a useful quantitative indicator of intensity of exposure and even duration of exposure was rarely addressed. Concerning type of exposure only quite crude and broad categories were used.

In ecological studies, although for the studied population the exposure - despite considerable variations in time - is similar with respect to carrier frequency, modulation etc. it is quite different between various types of transmitters and hence results are not easily generalized. The ecological studies are not conclusive with respect to brain tumors but provide some evidence for hematopoietic malignancies that need to be further pursued. Investigating residential exposure to RF EMFs from broadcasting stations poses severe methodological problems mainly due to the small size of the exposed population because high exposure levels occur only in a small band around the radiation sources. Due to the transition to digital television many TV broadcasting antennas with high power are or will be disconnected leaving us with changing exposure conditions. Because brain tumors have long latencies it is hardly possible to produce conclusive evidence in the near future.

Considering the discussion of the different investigations and the fact that most biases encountered tend to dilute a potential risk, the compiled evidence from occupational cohorts is compatible with a moderately increased risk of RF exposure. Because of the lack of actual measurements but observing that exposure above guideline levels must have been a rare event a precautionary approach must result in a reduction of occupational exposure levels and organizational measures to avoid over-exposure and also environmental exposure levels should be given greater attention. Although brain tumors are rare and the population attributable risk is low (assuming 13% of adults being occupationally exposed to RF fields as inferred from Berg et al. 2006, and assuming a relative risk of 1.3, about 4% of brain tumors can be attributed to RF exposure, i.e. 2,200 cases per years in the US).

CONCLUSIONS

- Only few studies of long-term exposure to low levels of RF fields and brain tumors exist, all of which have methodological shortcomings including lack of quantitative exposure assessment. Given the crude exposure categories and the likelihood of a bias towards the null hypothesis of no association the body of evidence is consistent with a moderately elevated risk.

- Occupational studies indicate that long term exposure at workplaces may be associated with an elevated brain tumor risk.

- Although in some occupations and especially in military jobs current exposure guidelines may have sometimes been reached or exceeded, overall the evidence suggest that long-term exposure to levels generally lying below current guideline levels still carry the risk of increasing the incidence of brain tumors.

- Although the population attributable risk is low (likely below 4%), still more than 2,000 cases per year in the US can be attributed to RF exposure at workplaces alone. Due to the lack of conclusive studies of environmental RF exposure and brain tumors the potential of these exposures to increase the risk cannot be estimated. However, these figures are theoretical as long as the evidence is as weak as it is for the time being.

V. ASSESSMENT OF EPIDEMIOLOGICAL EVIDENCE BY IEEE (C95.1 REVISION)

Introduction

Before 1988 C95 standards were developed by Accredited Standards Committee C95, between 1988 and 1990, the committee was converted to Standards Coordinating Committee 28 (SCC 28) under the sponsorship of the IEEE Standards Board. In 2001 IEEE approved the name "International Committee on Electromagnetic Safety (ICES)" for SCC 28. Subcommittee 4 of ICES Technical Committee 95 is responsible for the revision of standard C95.1 "IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz". There are five TC95 subcommittees: 1) Techniques, Procedures, and Instrumentation; 2) Terminology, Units of Measurements and Hazard Communication; 3) Safety Levels with Respect to Human Exposure, 0-3 kHz; 4) Safety Levels with Respect to Human Exposure, 3 kHz-300 GHz; 5) Safety Levels with Respect to Electro-Explosive Devices.

The recommendations in standard C95.1 are intended to protect against scientifically established adverse health effects in human beings resulting from exposure to radio frequency electromagnetic fields in the frequency range of 3 kHz to 300 GHz. A "scientifically established adverse health effects" is defined as: "A biological effect characterized by a harmful change in health that is supported by consistent findings of that effect in studies published in the peer-reviewed scientific literature, with evidence of the effect being demonstrated by independent laboratories, and where there is consensus in the scientific community that the effect occurs for the specified exposure conditions." It is interesting that this definition does not only demand the effect being demonstrated by independent laboratories but also that a consensus must be reached in the scientific community. This is a strange definition. When is a consensus reached? If more than 50% of scientists in the scientific community agree? Or must all agree? Usually this term is used to describe a situation where there is no open or covert dissent. In decisions theory demanding consent is criticized as a policy that results in the preservation of the status-quo.

It might be instructive to contrast this definition with IARCs (International Agency for Research on Cancer) characterization of sufficient evidence for carcinogenicity in experimental animals: "The Working Group considers that a causal relationship has been established between the agent or mixture and an increased incidence of malignant neoplasms

or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) in two or more independent studies in one species carried out at different times or in different laboratories or under different protocols", and the characterization of sufficient evidence in humans: "The Working Group considers that a causal relationship has been established between exposure to the agent, mixture or exposure circumstance and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence." Clearly these definitions are incompatible with the definition by IEEE.

The scientific rationale for the derivation of the exposure standard of IEEE is presented in Annex C and Annex B "Identification of levels of RF exposure responsible for adverse effects: summary of the literature" which is based on "critical reviews of studies within the IEEE/WHO RF literature database". In this commentary I will address chapter 9) Epidemiological Studies of RF Exposures and Human Cancer.

Evaluation of Cancer-Related Endpoints (RF Exposure)

In their 2006 revision of the standard C95.1 IEEE has assessed the evidence from epidemiology for cancer related endpoints in chapter B.7.3. The assessment relies mainly on the reviews of Bergqvist (1997), Moulder et al. (1999) and Elwood (2003). These reviews and the IEEE overview share the same deficiencies. The main lines of argumentation would be impossible in any other field of environmental health and closely resemble the strategy used to dismiss a power frequency exposure/childhood leukemia association. In the following paragraphs the assessment by IEEE will be discussed. The text of IEEE C95.1 is presented in italics as blocked citation. References within the text of the citations are found by the Rnnn and Bnnn numbers in the Annexes F and G of the standard document, but are also included in the reference section of this overview.

> *Cluster studies, such as the one performed in Sutton Coldfield in the U.K. in response to a cluster of leukemia and lymphoma in adults living close to an RF broadcasting transmitter (Dolk et al. [R624]), are inherently difficult to interpret because of the impossibility of assessing all of the effects that chance variation might have contributed to the cluster. In the initial Sutton Coldfield study, the authors correctly concluded that no causal association could be drawn between the presence of the cluster and RF exposure from broadcasting towers (Dolk et al. [R625]) (Cooper et al. [R760]). (IEEE C 95.1 – 2005, p.75)*

First of all the Sutton Coldfield study was no cluster study but an ecological investigation. It only was initiated by an unconfirmed report of a cluster of leukemia and lymphoma in the vicinity of this broadcasting transmitter but it proceeded independently of this initial report and used registry data of the population living within a radius of 10 km around the transmitter. The statement that such studies are "inherently difficult to interpret because of the impossibility of assessing all of the effects that chance variation might have contributed to the cluster" is ridiculous not only because the study is no cluster study but because it is impossible for any study to "assess all effects that chance variation might have contributed" to the endpoint under investigation. It is not mentioned that the study was supplemented by a larger investigation of another 20 high-power transmitters in Great Britain. The difficulties of interpreting ecological studies is related to the fact that potential confounders can only be related to a segment of the population but not to individuals and that in general duration and intensity of exposure are not known for individual members of the different strata. While evidence for an effect on brain tumor incidence from both studies (Dolk et al. 1997a, 1997b) is weak, there is consistent evidence for a relation to hematopoietic cancers. This evidence has been overlooked by the authors due to their wrong assumption about the relation between proximity to the transmitter and exposure.

> *Inconsistent effects have been reported between residential proximity to other RF broadcast towers and adverse health endpoints (Bielski [R267]) (Maskarinec et al. [R579]) (Selvin and Merrill [R823]) (Michelozzi et al. [R858]) (Altpeter et al. [R977]) (Hallberg and Johansson [R995], [R996]) (Boscolo [R1012]), although many of these studies have significant flaws in their study design (making them difficult to interpret). (IEEE C 95.1 – 2005, p.75)*

Although it is not stated what these "inconsistent effects" might be, the statement is flawed in more than this respect. First of all the study by Bielski (1994) is an occupational investigation and not about residential proximity to RF broadcast towers, second three of these investigations (Selvin et al. 1992; Maskarinec et al. 1994; Michelozzi et al. 2002) included leukemia as an endpoint with indications of an increased incidence consistent with the studies from Great Britain (Dolk et al. 1997a, 1997b) and Australia (Hocking et al. 1996). Note that the study by Selvin et al. (1992), as stated in section 10, intended to compare different methods to assess the relationship between a point source and diseases and did erroneously assume a monotonous relationship between exposure and distance from a transmitter. Correcting this error there seems to be an increased probability of childhood leukemia in areas receiving the highest exposure from the Sutro tower. The other three investigations (Altpeter

et al. 1995; Boscolo 2001; Hallberg & Johansson 2002) have nothing in common and hence cannot be inconsistent.

> *An increased incidence and mortality rate of childhood leukemia was reported in Australia with residential proximity to a specific RF broadcasting tower (Hocking et al. [R633]), although subsequent reanalysis of the data showed the results may have been influenced by other confounding variables within the study location (McKenzie et al. [R669]). (IEEE C 95.1 – 2005, p.75)*

This is another example how carelessly and sloppy the evidence is dealt with by the IEEE committee. The study of Hocking et al. (1996) was not about "proximity to a specific RF broadcasting tower" but about an area where three broadcasting towers are located. While there is always the possibility of confounders influencing results of an epidemiologic investigation, the 'reanalysis' of McKenzie et al. (1998) is seriously flawed and cannot support the cited statement. Hocking et al. (1996) combined the districts near the broadcasting area and those further away based on homogeneity analyses, while McKenzie et al. (1998) omitted one area with high incidence (and highest exposure) based on inspection of data. Any statistical analysis subsequent to such data picking is useless.

> *While scattered reports of adverse health effects associated with occupational exposure to RF do exist (Demers et al. [R36]) (Kurt and Milham [R68]) (Pearce [R110]) (Speers et al. [R125]) (Thomas et al. [R128]) (Pearce et al. [R199], [R211]) (Hayes et al. [R207]) (Cantor et al. [R268]) (Davis and Mostofi [R563]) (Tynes et al. [R570], [R605]) (Grayson [R592]) (Richter et al. [R747]) (Holly et al. [R838]) these studies are largely inconsistent with each other in terms of the adverse health endpoints affected, and often show no clear dose response with RF exposure. Many have serious flaws in their study design, contain limited or insufficient RF exposure assessment, and are generally inconsistent with the absence of findings of an association from other occupational studies (Tornqvist et al. [R131]) (Coleman [R142]) (Lilienfeld et al. [R146]) (Robinette and Silverman [R147], [R148]) (Siekierzynski et al. [R151], [R152]) (Wright et al. [R213]) (Coleman et al. [R214]) (Muhm [R506]) (Czerski et al. [R542]) (Hill [R568]) (Lagorio et al. [R616]) (Kaplan et al. [R647]) (Morgan et al. [R701]) (Gallagher et al. [R822]) (Groves et al. [R853]) (Wiklund [R1013]) (Armstrong et al. [R1014]). (IEEE C 95.1 – 2005, p.75)*

Even allowing for restrictions of space for a discussion of the evidence, greater nonsense has not been produced so far in this field as condensed in these two sentences. Putting higgledy-piggledy all sorts of studies together and then wondering about endpoints being inconsistent is an intellectual masterpiece. Of the occupational studies mentioned, three (Thomas et al. 1987; Speers et al. 1988; Grayson 1996) were about brain cancer, three about hematopoietic cancers

(Pearce et al. 1985; Kurt & Milham 1988; Pearce 1988), two about testicular cancer (Hayes et al. 1990; Davis & Mostofi 1993), one about male (Demers et al. 1991) and two about female breast cancer (Cantor et al. 1995, Tynes et al. 1996) the latter including other cancers as well, and one about intraocular melanoma (Holly et al. 1996). Three further studies (Pearce et al. 1989; Tynes et al. 1992; Richter et al. 2000) investigated several or all malignancies. These studies differ not only in endpoints, study type (cohort, case-control, and cluster) but also in the methods of exposure assessment. Ignorance of the IEEE reviewers is underlined by the compilation of studies characterized by an "absence of findings of an association". Not only did several of these studies indeed indicate an association of cancer risk with EMF exposure (Lilienfeld et al. 1978; Robinette et al. 1980; Tornqvist et al. 1991; Armstrong et al. 1994; Lagorio et al. 1997; Groves et al. 2002) but two were no epidemiologic studies at all (Siekierzynski et al. 1974; Czerski et al. 1974) and several were rather addressing ELF exposure (Tornqvist et al. 1991; Wright et al. 1982; Coleman et al. 1983; Gallagher et al. 1991) and one (Wiklund 1981) was a cluster study in the telecommunication administration with uncertain type of exposure. Simply confronting studies finding an effect with others that were 'negative' is scientifically flawed and permits neither the conclusion that there is nor that there is no association between exposure and cancer risk. Even if all studies would have applied the same method, assessed the same endpoint and used the same exposure metric, studies reporting a significantly increased cancer risk are not outweighed by others that did not.

> *While micronuclei formation in workers occupationally exposed from broadcast antennas has been reported (Garaj-Vrhovac [R757]) (Lalic et al. [R791]), these findings were not verified in a larger study of more than 40 Australian linemen exposed under similar conditions (Garson et al. [R186]). (IEEE C 95.1 – 2005, pp.75-76)*

It goes without saying that also this statement is wrong. Garson et al. (1991) did not investigate micronuclei formation, their workers were considerably shorter exposed and it were not more than 40 linemen but 38 radio-lineman.

> *No clear association could be established between occupational exposures of parents to a number of agents, including RF, and effects (neuroblastoma) in their offspring (Spitz and Johnson [R289]) (De Roos et al. [R798]). (IEEE C 95.1 – 2005, p.76)*

What is meant by 'no clear association' is obscure. Spitz and Johnson (1985) found a significantly increased risk after paternal occupational exposure to electromagnetic fields, and also De Roos et al. (2001) found several jobs with paternal as well as maternal exposure to

EMFs associated with an elevated risk for neuroblastoma in their children. However, broad groupings of occupations with ELF, RF EMF, as well as ionizing radiation (!) exposure did not reveal an increased risk.

> *One study reported a slight excess in brain tumors associated with combined exposure to RF and other exposures associated with electrical or electronic jobs, but not with RF alone (Thomas et al. [R128]). A study of a Polish military cohort reported a substantial excess of total cancer and several cancer sub-types with jobs associated with RF exposure (Szmigielski [R578]), (Szmigielski and Kubacki [R982]), although questions have been raised about severe bias in the exposure assessment of this study (Elwood [R665]) (Bergqvist [R1015]) (Stewart [R1133]). Studies by Milham of U.S. amateur radio operators reported an excess in one of nine types of leukemia assessed (see [R101], [R102], [R209], [R215], and [R569]), but not for total tumors, total leukemia, or brain tumors, and potential confounding factors might have included exposure to soldering fumes, degreasing agents and over-representation of a particular social class. (IEEE C 95.1 – 2005, p.76)*

Again the evidence is incorrectly summarized for all cited investigations. Thomas et al. (1987) found a significantly elevated risk for brain tumors among all men exposed to RF fields and in particular in those exposed for 20 or more years. There were indications that this elevated risk is due to a subgroup with electrical or electronics jobs. The group of those exposed in other jobs is heterogeneous and may contain subjects with low or no exposure (e.g. some groups of welders) and therefore lack of an association could be due to a dilution effect from exposure misclassification.

As mentioned in section 10 criticism of the Polish military cohort study about exposure assessment is unfounded. Bergqvist (1997), Elwood (1999) and Stewart (2000) criticized that the military health board assessed a number of potential risk factors only for cancer cases. However, they overlooked that the study was a cohort and not a case-control study and that at no stage information about these factors entered the analysis and therefore couldn't affect the results in any way.

The study by Milham (1988a, 1988b) of radio amateur operators revealed a significantly increased standardized mortality ratio (SMR) for acute myeloid leukemia while the overall mortality and cancer mortality was significantly reduced relative to the country mortality rates. As mentioned in section 10 this points to a 'healthy worker' effect as well as to an influence of life-style factors (mortality related to smoking and overweight were reduced). From the mentioned nine types of leukemia three with expectancies below one and no case observed couldn't be assessed, from the six remaining types five had elevated SMRs with AML, the most frequent type in adults, being significantly elevated.

The last portion of the IEEE review of epidemiology studies is dedicated to mobile phone investigations that are discussed in another contribution.

The following citation presents the IEEE summary in its full length:

> *The epidemiological evidence to date does not show clear or consistent evidence to indicate a causal role of RF exposures in connection with human cancer or other disease endpoints. Many of the relevant studies, however, are weak in terms of their design, their lack of detailed exposure assessment, and have potential biases in the data. While the available results do not indicate a strong causal association, they cannot establish the absence of a hazard. They do indicate that for commonly encountered RF exposures, any health effects, if they exist, must be small. Even though epidemiological evidence cannot rule out a causal relationship, the overall weight-of-evidence is consistent with the results of the long term animal studies showing no evidence of physiological, pathological or disease-specific effects. (IEEE C95.1 - 2005; pp.76-77)*

As already pointed out earlier (Kundi 2006) there is an intolerable tendency in the past years that confronted with an undeniable epidemiologic evidence of an association between an agent and adverse health effects such as cancer, interested parties take their resort to the concept of causality based on the wrong assumption evidence to "indicate a causal role" is a lot more difficult to provide. Unprecedented, however, is the notion of "a strong causal association". Whatever the meaning of this exceptional statement, the conclusion that, if health effects of commonly encountered RF exposures exist, they must be small, is wrong. To the contrary: considering the "lack of detailed exposure assessment" and other potential biases that predominantly lead to an underestimation of the risk, the evidence points to a quite substantial risk. While the animal studies reviewed in another section of the IEEE standard document cannot be discussed here it should be underlined that they are generally insufficient to support either an increased risk or the lack of health relevant effects. Therefore they cannot be used in a weight-of-evidence statement as has been made by IEEE, that there is no evidence for adverse health effects of RF exposure.

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