

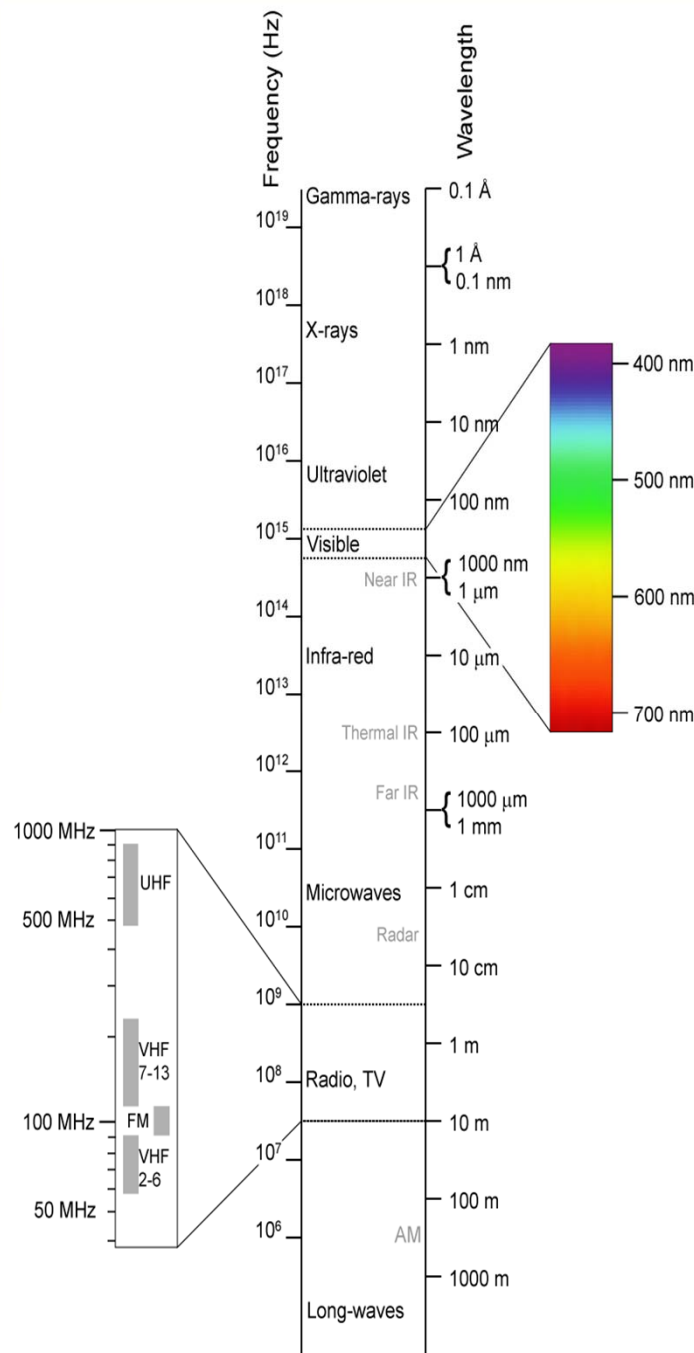
Cellular Telephones and Brain Tumors

Peter D. Inskip, Sc.D.
Division of Cancer Epidemiology & Genetics
National Cancer Institute

Background

- Issue comes to widespread public attention in January of 1993 following anecdotal report on TV show
- **Context:** Novel technology
 - Rapid increase in use
 - Radiofrequency (RF) “radiation”
 - Limited information re: RF radiation risks
 - Etiology of brain tumors largely unknown
- Congressional hearings in February 1993
- NCI adds a cellular-phone component to a planned case-control study of brain tumors

Electromagnetic Spectrum



Digital phones
(up to 1900 MHz)

Early analog phones
(800-900 MHz)

Biological Effects of Radiofrequency Radiation

- Energy of a radiofrequency (RF) wave from a cellular telephone is billions of times lower than the energy of an x-ray photon
- RF radiation is insufficiently energetic to break molecular bonds or ionize molecules
- At high power levels, RF radiation can cause heating, but biological effect from cellular phone use unlikely to be thermal
- No consistent experimental evidence of carcinogenicity or genotoxicity
- Mechanism by which RF radiation might cause cancer?

Number of Wireless Subscribers in U.S. (1984-2007)



Brain/CNS Tumors

Type	Incidence Rate (per 100,000)	Usual Behavior
Glioma	6.5	malignant
Meningioma	5.4	benign
Acoustic neuroma	1.3	benign

NCI Study – Methods

- Hospital-based, case-control study
- 3 hospitals (Phoenix, Pittsburgh, Boston)
- 782 newly-diagnosed cases (489 glioma, 197 meningioma, 96 acoustic neuroma)
- 799 matched controls
- Interview about use of cellular phones
- Data collection from 1994 to 1998

The New England Journal of Medicine

© Copyright, 2001, by the Massachusetts Medical Society

VOLUME 344

JANUARY 11, 2001

NUMBER 2



CELLULAR-TELEPHONE USE AND BRAIN TUMORS

PETER D. INSKIP, Sc.D., ROBERT E. TARONE, Ph.D., ELIZABETH E. HATCH, Ph.D., TIMOTHY C. WILCOSKY, Ph.D.,
WILLIAM R. SHAPIRO, M.D., ROBERT G. SELKER, M.D., HOWARD A. FINE, M.D., PETER M. BLACK, M.D.,
JAY S. LOEFFLER, M.D., AND MARTHA S. LINET, M.D.

Cell-Phone Use and Risk of Glioma

Cumulative

Use (hr)	Controls	Cases	OR	95% CI
never/rarely	625	398	1.0	
< 13	55	26	0.8	0.4 - 1.4
13 to 100	58	26	0.7	0.4 - 1.3
> 100	54	32	0.9	0.5 - 1.6
> 500	27	11	0.5	0.2 - 1.3

Cell-Phone Use and Risk of Glioma: Laterality of Tumor and Phone Use

Tumor	Phone Use*		P-value**
	Left	Right	
Left	8	18	0.77
Right	10	17	

* Use for ≥ 6 months before tumor diagnosis

** Test for independence

Main Findings

- **No association between incidence of glioma and level of use of cell phone**
- **Laterality of cancer not related to laterality of phone use**
- **Similar findings for meningioma & acoustic neuroma**

Strengths

- **Incident, histologically-confirmed cases**
- **Rapid case ascertainment**
 - **Relatively few proxy interviews**
- **High participation rates (92% for cases, 86% for controls)**
- **Large sample size for glioma**
- **Use of imaging and surgical reports to determine tumor location**

Limitations

- **Small number of long-term, heavy users**
- **Cannot rule out small risks**
- **Reliance on interviews taken after tumor diagnosis to assess cell phone use**
 - **potential for imperfect recall (as in all case-control studies)**
- **Changes in cellular technology**



Changes in Cellular Networks and Phones

- **Analog versus digital**
 - First cell phones were analog
 - Digital service began in the U.S. in 1992; earlier in Europe
 - Current cell phones are digital
 - Digital phones emit less RF energy per unit time
 - Adaptive power control
- **Higher density of base station antennas**
- **Higher operating frequencies**

Other Early Studies of Cell Phones and Glioma

Study	Cases	Association?
Case-control study in USA *	469	No
Cohort study in Denmark **	127	No

* Muscat et al. (*JAMA* 2000)

** Johansen et al. (*JNCI* 2001)

Next Generation of Studies

- Expanded Danish Cohort Study
- INTERPHONE Case-control Study

Expanded Danish Cohort Study

- 420,095 persons with 1st cellular phone subscription between 1982 and 1995
- Followed through 2002 for cancer incidence
- Compared incidence with general population

	SIR	95% CI
Glioma	1.01	0.89 - 1.14
Meningioma	0.86	0.67 - 1.09
Acoustic neuroma	0.73	0.50 - 1.03

- No increases in brain tumor incidence among 10+ year subscribers

INTERPHONE Study

- **International case-control study, led by IARC**
- **13 population-based cancer registries**
 - **Countries where cell phone use preceded that in US**
- **Year of diagnosis: 2000-2004**
- **Age at diagnosis: 30-59 years**
- **2,708 glioma cases**
- **2,409 meningioma cases**
- **Some centers also enrolled patients with acoustic neuroma & parotid gland tumors**

INTERPHONE Study

- Denmark
- Finland
- Norway
- Sweden
- United Kingdom (UK)
- Germany
- France
- Italy
- Israel
- New Zealand
- Australia
- Japan
- Canada

Glioma – Pooled Analysis

- Denmark, Finland, Norway, Sweden, UK
- 1,521 glioma patients, 3,301 controls
- Glioma: OR=0.78 (CI: 0.68-0.91)
- No overall increase in risk for years since 1st use, lifetime years of use, number of calls, hours of use, or analog vs. digital phones
- Slightly increased OR for use of phone on same side of head for more than 10 years (OR=1.39; CI:1.01-1.92)

Lahkola et al. *Int J Cancer* (2006)

Meningioma – Pooled Analysis

- 1,209 meningioma cases, 3,299 controls
- OR (regular use)=0.76; CI: (0.65-0.89)
- Risk not increased in relation to years since first use, lifetime years of use, cumulative hours of use, number of calls or laterality of tumor relative to laterality of phone use
- Findings similar for analog and digital phones

Lahkola et al. *Int J Epidemiol* (2008)

Acoustic Neuroma – Pooled Analysis

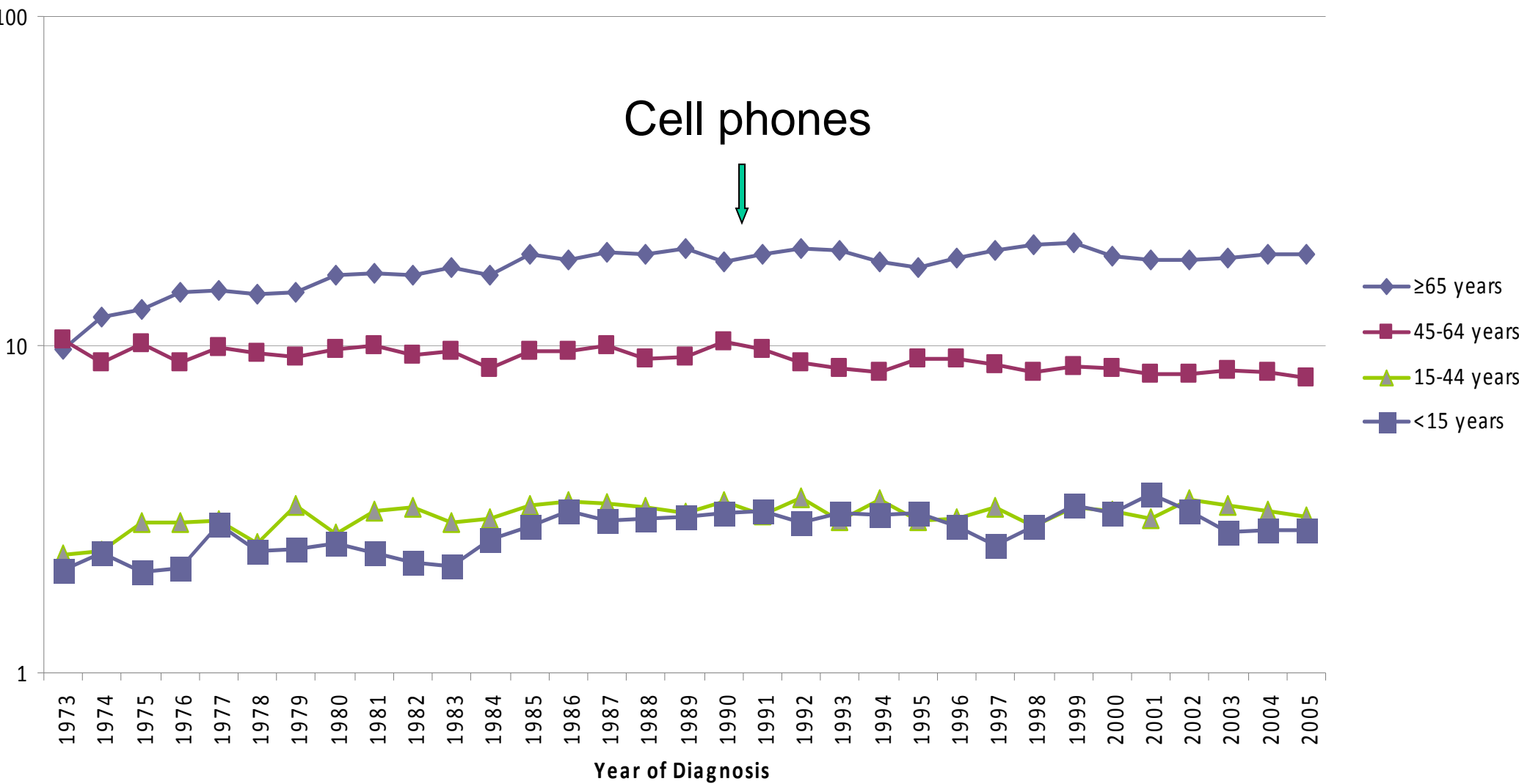
- 678 cases, 3,553 controls
- Overall, risk not associated with regular use (OR=0.9; CI:0.7-1.1), duration of use, lifetime cumulative hours of use or number of calls, phone use for ≥ 10 years or for analog vs. digital phones separately
- OR elevated for use of phone on same side of head as tumor for ≥ 10 years (OR=1.8; CI: 1.1-3.1)

Schoemaker et al. *Br. J Cancer* (2005)

Related Topics

- **Time trends in brain cancer incidence**
- **Studies of occupational exposure to radiofrequency radiation and cancer**
- **Childhood use of cellular phones and cancer**
- **Studies of cellular phones in relation to outcomes other than brain tumors**

Trends in Brain Cancer Incidence By Age, 1973-2005 (SEER)



Occupational Studies

Morgan et al. (2000)

- 195,775 Motorola workers engaged in manufacturing & testing cellular phones (1976-96)
- RF exposure estimated by job exposure matrix
- No association between RF exposure & mortality due to brain cancer
 - No information on personal cell phone use

Occupational Studies (cont'd)

Groves et al. (2002)

- 40,581 Navy veterans of Korean war
- Potential exposure to high-intensity radar
- No evidence of increased mortality due to brain cancer, either in the entire cohort (SMR=0.9), or in high-exposure occupations (SMR=0.7; CI: 0.5-1.0)

Childhood Use of Cellular Phones and Cancer

- Possible differences in sensitivity of children and adults?
- No published epidemiologic studies of cell phone use in relation to childhood exposure
- Ongoing case-control study in Denmark, Norway, Sweden & Switzerland
- Ongoing Danish and Norwegian childhood cohort studies (N=200,000 children)

Other Outcomes and Cellular Telephone Use

Other Cancers

- Non-Hodgkin lymphoma
- Parotid gland tumors
- Uveal melanoma

Other conditions

- Cognitive function
- Electrical activity in brain
- Sleep
- Interference with pacemakers
- Motor vehicle accidents

Summary

- Brain cancer incidence trends for brain cancer unrelated to cell phone use
- Most analytic studies indicate little or no overall increased risk of brain tumors within first 10 years of use
- No consistent subgroup findings but need larger numbers of longer-term users to evaluate different exposure metrics, latency, laterality, etc.
- Multiple comparisons → expect chance findings
 - Need to evaluate consistency within and among studies

Summary (cont'd)

- Further studies are needed to detect longer-term risks and risks to children
- Insight may come from ongoing analyses of overall INTERPHONE study, and from northern European case-control study of childhood cancer