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# Summary and Results of the April 26-27, 1993 Radiofrequency Radiation Conference

Volume 2: Papers





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## Summary and Results of the April 26-27, 1993 Radiofrequency Radiation Conference

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### ABSTRACT

On April 26 and 27, 1993, the U.S. Environmental Protection Agency (EPA) Office of Air and Radiation and Office of Research and Development held a conference to assess the current knowledge of biological and human health effects of radiofrequency (RF) radiation and to address the need for and potential impact of finalization of federal guidance on human exposures to RF radiation. More than 200 people attended the conference. Attendees represented the federal government, academia, the private sector, trade associations, the media, and the public. Plenary papers presented at the meeting focused on current research findings on a variety of topics, including exposure assessment, dosimetry, biological effects, epidemiology, the basis for exposure limits, and emerging health issues. Panel discussions focused on identifying key scientific information needs for and the policy implications of the development of further EPA guidance on human exposures to RF radiation. This document, Volume 2, provides the plenary papers presented by speakers. Volume 1, under separate cover, provides a record of much of the information presented at the conference, outlines key recommendations provided to EPA by conference participants, and presents the EPA strategy for addressing RF radiation.

Two key recommendations for EPA emerged from the conference: (1) develop RF radiation exposure guidance as soon as possible, and (2) conduct additional research in a number of areas, particularly with respect to the potential for "nonthermal" effects. These recommendations were considered by EPA in its decision to proceed with the development of guidelines on human exposure to RF radiation and to develop a longer term strategy to address remaining issues. Part of this strategy has involved creating an inter-agency work group and requesting the National Council on Radiation Protection (NCRP) to assess several remaining issues. Information provided at the conference also was used as a basis for EPA comments to the Federal Communications Commission (FCC) 1993 proposal to adopt the RF radiation exposure guidelines developed in 1992 by the American National Standards Institute (ANSI) and the Institute for Electrical and Electronics Engineers (IEEE).

### A REVIEW OF RADIOFREQUENCY ELECTRIC AND MAGNETIC FIELDS IN THE GENERAL AND WORK ENVIRONMENT: 10 kHz to 100 GHz\*

Edwin D. Mantiply\*\* Samuel W. Poppell Julia A. James

#### ABSTRACT

We have plotted data from a number of studies on the range of radiofrequency (RF) field levels due to a variety of environmental and occupational sources. This work is organized into standard frequency bands from very-low frequency (VLF) to super-high frequency (SHF). Electric field values range from micro- to kilovolts per meter. Most of the reported electric fields range from 0.1 to 1000 volts/meter (V/m). The strongest fields observed are near industrial induction and dielectric heaters, close to the radiating elements or transmitter leads of high power antenna systems and in front of onboard aircraft radars. Hand-held transmitters can produce near electric fields of hundreds of volts per meter. Peak fields from air traffic radars in the general urban environment are about 10 V/m and about 300 times greater than the true root-mean-square (rms) field strength when rotation and pulsing are factored in. Loran navigational and amateur transmissions can be modulated at extremely-low frequencies. Sources used for heating are likely to be amplitude modulated at harmonics of the power frequency. Sources included in this review are the following: Coast Guard navigational transmitters; a Naval VLF transmitter at Lualualei, Hawaii; computer video displays; induction stoves or rangetops; industrial induction and dielectric heaters; radio and television broadcast transmitters; amateur and CB transmitters; medical diathermy and electrosurgical units; mobile and hand-held transmitters; cordless and cellular telephones; microwave ovens; microwave terrestrial relay and satellite uplinks; and police, air traffic, and aircraft onboard radars.

#### INTRODUCTION

In response to the question "Who is exposed to what?", this paper graphically presents an overview of RF electric and magnetic fields measured in various environmental, occupational, and product evaluation studies. The scope is wide in terms of the type of sources included. Any type of source causing potential exposures can be included. However, the scope is narrow with respect to the metrics of exposure covered. No discussion of dosimetry, coupling of fields to induce body currents, or applicability of various exposure guidelines, is undertaken.

In addition to field strength, the time variation or modulation and spatial character of fields are reviewed. For example, data on three exposure milieu are included for broadcast stations. First, a range of general environmental levels; second, the range of field values found on the ground or at buildings in the immediate vicinity of the transmitting antenna; and third, possible exposure values for an individual climbing the antenna tower are described.

This paper is intended to be an introduction and bibliography to RF levels. Earlier reviews contain more descriptive information on how fields are measured, calculated, and shielded [Stuchly, 1977; Stuchly and Mild, 1987; Mild and Lovstrand, 1990; Joyner, 1988; Hankin, 1986].

<sup>\*</sup> Key words: nonionizing radiation, exposure. This paper was updated in November 1993.

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The review is organized into seven standard radiofrequency bands and covers the sources shown in Table 1. Figure 1 is a summary plot showing the format of presentation without identifying the boxes that show the field and frequency ranges for the various sources covered; Figures 2 through 8 give the results for each band with the boxes identified.

Adjectival Band Designation	Abbre- viation	Frequency Range	Sources Included	
Very-low frequency	VLF	10* to 30 kHz	omega navigational transmitters, a Navy communication transmitter, video displays, induction stoves	
Low frequency	LF	30 to 300 kHz	loran navigational transmitters	
Medium frequency	MF	300 to 3000 kHz	AM broadcast, 160 meter amateur, induction heaters, electrosurgical units	
High frequency	HF	3 to 30 MHz	international broadcast, amateur and CB, dielectric heaters, shortwave diathermy	
Very-high frequency	VHF	30 to 300 MHz	FM broadcast, VHF television, mobile and hand-held transmitters, cordless telephones	
Ultra-high frequency	UHF	300 to 3000 MHz	UHF television, cellular telephones, microwave ovens and diathermy, air traffic radars	
Super-high frequency	SHF	3 to 30 GHz**	microwave relay, satellite uplinks, aircraft onboard radar, police radar	

TABLE I. Frequency Bands and Sources Included	l in	Review
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\* The standard start frequency for VLF is 3 kHz; 10 kHz is used here.

\*\* No data on sources between 30 and 100 GHz was found.

#### VERY-LOW FREQUENCY, 10 kHZ TO 30 kHZ

The wavelength for this frequency range varies from 30 km at 10 kHz to 10 km at 30 kHz. Antennas designed to transmit at these long wavelengths are large structures driven at high voltage. The typical antenna is similar to that for a standard AM broadcast station where the entire tower acts as the antenna. However, in contrast to most AM towers, many VLF antennas use extended wire structures connected to the top of a tower or transmitter lead (feed line) to increase the effective height of the antenna. In all cases, the radiating structure is insulated and driven at some high radiofrequency potential referenced to a ground radial system. Transmitting systems in the VLF frequency range that have been studied in some detail include omega navigational systems and the VLF submarine communication system at Lualualei, Hawaii. Finally, near field sources such as video displays and induction heaters generate VLF electric and magnetic fields in their immediate vicinities. Figure 2 displays the range of field strengths measured for some VLF sources.

#### **Omega Navigational Transmitters**

There are eight omega very-long-distance navigational transmitters in the world. Two are in the United States -- one in North Dakota and one in Hawaii [Gailey, 1987]. These VLF transmitters switch between frequencies from 10.2 to 13.6 kHz in a repeating 10 second cycle. The transmission is a series



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Fig. 1. Summary chart of field levels detailed in Figures 2 through 8. Each box represents a field strength and frequency range for a particular source and region of possible exposure. The vertical axes for electric and magnetic fields and equivalent power density are scaled so that the three values found on a horizontal line correspond to the fields and power density of a plane electromagnetic wave propagating in free space where the ratio of the electric to the magnetic field is 377 ohms. The vertical scales are kept constant in all figures. Electric and magnetic field measurements are plotted as lines slanted in opposite directions so that a cross hatched region indicates a range of field magnitudes having a ratio similar to the value in free space.

ω



Fig. 2. Very-low frequency fields. The first block shows the range of electric and magnetic fields seen near the omega transmitting antenna in North Dakota. The lower values was measured at 640 m from the tower and the higher values were found at about 12 m from the tower. The video displays box is the range of VLF fields measured 30 cm in front of VDT's in a large number of studies. The Lualualei box shows the range of fields seen in the community surrounding the Lualualei Naval VLF transmitter in Hawaii. The induction stove box shows fields measured 30 cm from induction rangetops.

of eight single-frequency sinusoidal carriers switched on for 0.9 to 1.2 seconds with a pause of 0.2 seconds between each carrier. The drive voltage on omega antennas is about 250 kilovolts. For the North Dakota station, the measured rms electric field varied smoothly along one radial from 66 volts/meter (V/m) at 640 m to 4400 V/m at 12 m from the tower base. The rms magnetic field varied from 20 milliamp/meter (mA/m) at 640 m to 2.9 amp/meter (A/m) at 11 m from the tower. The Hawaii omega station antenna is more complex, and so are the field variations. For example, outside the station building, reported electric fields varied from 57 to 938 V/m and magnetic fields varied from 1.2 to 4.4 A/m. The maximum measured magnetic field at Hawaii was 18 A/m near the main feed line. Earlier investigators reported magnetic fields of from 0.2 to 6.2 A/m in the transmitter building and near the feed line [Guy and Chou, 1982].

#### VLF Transmitter at Lualualei, Hawaii

The U. S. Navy operates a VLF transmitter at Lualualei, Hawaii on a frequency of 23.4 kHz [Mantiply, 1992]. The signal is frequency modulated so that it appears to be a constant sinusoidal carrier for field measurement purposes. Outside the station boundary and in the surrounding community, the measured electric fields varied from 0.15 to 82 V/m and the magnetic field varied from 2.5 to 99 mA/m. These measurements were made at distances of approximately 800 m to 7 km from the transmitting towers. On site measurements by the Navy in 1982 showed that the electric field varied from 972 V/m to 700 V/m between about 80 and 150 m from the antenna. Measured magnetic fields in the transmitter building and near the feed line varied from 0.11 to 14 A/m [Guy and Chou, 1982].

#### Video Displays

The common video display using a CRT generates a sawtooth waveform VLF magnetic field. This field is used to horizontally sweep the electron beam across the screen. VLF electric fields are also generated by the flyback transformer. The fundamental frequency of these fields is between 15 and 35 kHz and harmonics exist up to several hundred kilohertz. Many studies and reviews have been made of fields near video displays [Tell, 1990; Boivin, 1985; Mild and Sandstrom, 1992; Tofani and D'Amore, 1991; Stuchly et al., 1983; Walsh et al., 1991; Jokela et al., 1989; Schnorr et al., 1991; Kavet and Tell, 1991; Charron, 1988; Marha et al., 1983; Guy, 1987]. Most studies have made this measurement 30 cm (1 foot) in front of the screen center. Reported VLF electric fields at 30 cm range from 0.22 to 52 V/m; mean values reported by different investigators vary from 0.83 to 12.5 V/m. Reported VLF magnetic fields measured at 30 cm range from 0.26 to 170 mA/m; mean values reported vary from 20 to 85 mA/m. Greater VLF fields at the same distance can be found to the sides and rear of video displays.

#### Induction Heating Stoves

Induction heating stoves are home appliances that generate a magnetic field at tens of kilohertz to heat food by the induction of eddy currents in cooking utensils. Electric and magnetic fields have been measured near two stoves heating a variety of utensils [Stuchly and Lecuyer, 1987]. At a distance of 30 cm from the stove, electric fields averaged 4.3 to 4.9 V/m and magnetic fields varied from 0.7 to 1.6 A/m.

#### LOW FREQUENCY, 30 kHZ TO 300 kHZ

#### **Loran Navigational Transmitters**

Loran navigational transmitters emit a pulsed signal centered at 100 kHz. Each transmitter generates a unique pulse train repeating at 10 Hz [Gailey, 1987]. Depending on the pulse train, instantaneous peak fields vary from 11 to 18 times greater than the rms fields reported here. Electric and magnetic fields were measured at 9 different loran stations. Electric fields varied from 28 to 350 V/m and magnetic fields varied from 0.6 to 2.9 A/m at locations 3 to 4 m from the tower base or feed point. At a distance of 300 m the electric field varied from 3 to 9 V/m and the magnetic field varied from 6 to 41

mA/m. Maximum fields were generally measured near the antenna insulator or tuning coils. At eight stations, the maximum electric field varied from 463 to 2830 V/m and the maximum magnetic field varied from 3.8 to greater than 10 A/m. Magnetic fields up to 52 A/m near loran feeds have been reported [Guy and Chou, 1982]. Figure 3 summarizes low frequency fields near loran navigational transmitters.

#### MEDIUM FREQUENCY, 300 kHZ TO 3 MHZ

The medium frequency range from 300 kHz to 3 MHz has associated wavelengths of 1000 to 100 m. AM standard broadcast operates from 535 to 1605 kHz with wavelengths of 560 to 190 m. Amateur radio operators also transmit in the MF band at 1.8 to 2.0 MHz in the 160 meter band. Industrial and medical sources also operate at MF. Figure 4 summarizes fields in the medium frequency band.

#### **AM Standard Broadcast**

Studies of general population exposure in the United States by the Environmental Protection Agency in the late 1970's suggest that approximately 3 % of the urban population is exposed to electric fields greater than 1 V/m due to AM broadcast. Ninety-eight percent of the population is exposed to greater than 70 mV/m and the median exposure is about 280 mV/m [Hankin, 1986].

Recently, electric and magnetic fields were measured near eight AM broadcast towers [Mantiply and Cleveland, 1991]. The fields were measured at 1 to 100 m from the center of each tower base. One station operated at the maximum power of 50 kilowatts (kW); three stations transmitted at approximately 5 kW; and the remaining four stations were 1 kW transmitters. Fields were typically measured along three radials at each station. At distances of 1 or 2 meters, electric field values varied from 95 to 720 V/m and magnetic fields were from 0.1 to 1.5 A/m. At 100 m from the tower, electric fields varied from 2.5 to 20 V/m; magnetic, from 7.7 to 76 mA/m.

Fields were measured close to five AM towers in the Honolulu, Hawaii area [U.S. EPA, 1985]. Accessible regions near the tower base or tuning network were probed for maximum electric and magnetic fields. Maximum electric fields at the five towers varied from 100 to 300 V/m and maximum magnetic fields varied from 0.61 to 9.3 A/m. Magnetic fields of up to 14.4 A/m have been reported at about 2 feet from an antenna tuning coil at the base of an AM tower [Wang and Linthicum, 1976]. Electric fields up to 1170 V/m were measured at 2 m above ground and about 3 cm from the surface of one AM tower [Tell et al., 1988].

Special studies of AM field strengths at residences and at a school near AM radio stations have been made in Spokane, Washington and Honolulu, Hawaii [Tell et al., 1988; U.S. EPA, 1985]. In Honolulu, measurements were made at highrise condominiums adjacent to an AM broadcast tower. Electric fields at a recreational area outside on the roof of one of these buildings were typically 100 to 200 V/m, and the AM magnetic field was 120 mA/m. Indoors, in a thirtieth floor apartment, the electric field was 2 to 3 V/m and the magnetic field was 240 mA/m. Electric and magnetic fields were measured inside and outside a single family house in Spokane near a 50 kW AM station. At locations outside where the fields did not appear to be perturbed, electric fields varied from 9 to 19 V/m. Clearly perturbed electric fields inside the house varied from 1 to 55 V/m. Magnetic fields were also measured inside an elementary school in Spokane approximately 100 m from the same AM station. Electric fields in the school varied from 1 to 28 V/m and magnetic fields varied from 22 to 470 mA/m. Unperturbed electric and magnetic fields at the school were estimated to be 15 V/m and 40 mA/m. Apparently, both medium frequency electric and magnetic fields due to AM broadcast can be either increased or decreased in the indoor environment.



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Fig. 3. Low frequency fields near loran navigational transmitters. The upper box shows the range of rms fields measured at 9 loran stations at 3 to 4 m from the tower base or feed line. The lower box shows the range of fields at 300 m.

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Fig. 4. Medium band fields. The lower box shows the range of electric field exposure due to AM broadcast for about 95 percent of the U. S. urban population. The range of fields seen near eight AM broadcast towers at 1 meter and at 100 meters is plotted above the population exposure range. The range of fields measured directly beneath several amateur 160 meter band antennas is shown on the right. The range of fields seen in several studies of exposure for induction heater operators is on the left.

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Standard AM broadcast uses double-sideband amplitude modulation at audio frequencies. Measurement of nine different AM signals in Las Vegas, Nevada showed ELF modulation values from 4 to 30 % in the frequency range of 3 to 100 Hz [Mantiply, 1990].

#### Amateur 160 Meter Band

Amateur radio operators can transmit up to 1.5 kW in the 160 meter wavelength band from 1.8 to 2.0 MHz. Electric and magnetic fields in this band were measured at three amateur radio installations [Cleveland et al., 1991]. These measurements were made outdoors at 1 or 2 meters above ground beneath active antenna wires. The operator set the transmitter for a constant carrier at 1.95 MHz. Beneath an open line "modified T" antenna feed operating at 500 watts, electric fields varied from 52 to 240 V/m and magnetic fields varied from 37 to 310 mA/m. Beneath an "inverted V" dipole operating at 100 watts the electric field varied from 0.7 to 5.4 V/m, and the magnetic field varied from 4 to 100 mA/m. Beneath another 160 meter dipole antenna operated at 80 watts, the electric field varied from 5 to 22 V/m and the magnetic field varied from 13 to 78 mA/m.

#### **Induction Heaters**

Induction (eddy current) heaters are used in industry to heat metals or semiconductors by generating a strong alternating magnetic field inside a coil. The range of frequencies can be from 50 Hz to 27 MHz. Lower frequency units produce stronger magnetic fields that also penetrate and heat the material more deeply. Higher frequencies are used for surface heating. The strongest magnetic fields measured have been for heaters operating at frequencies below 10.3 kHz, but these frequencies are outside the scope of this review [Stuchly and Lecuyer, 1985; Mild and Lovstrand, 1990]. In 5 studies [Aniolczyk, 1981; Centaur, 1982; Stuchly and Lecuyer, 1985; Conover et al., 1986; Andreuccetti et al., 1988] measurements were made near medium frequency induction heaters operating from 250 to 790 kHz. These fields vary greatly over small distances and with the type of unit and process. Typically, the electric field may decrease from 1000 to 100 V/m and the magnetic field decreases from 20 to 0.5 A/m as distance from the coil is increased from 20 to 100 cm. Reported electric and magnetic field exposure for the operator vary from 2 V/m to 8.2 kV/m and 0.1 to 21 A/m. These field values are not corrected for duty cycle. It is likely that radiofrequency induction heater fields are amplitude modulated at multiples of the power frequency.

#### **Electrosurgical Units**

Medical electrosurgical units operate from 0.5 to 2.4 MHz with significant harmonics and spurious frequencies up to 100 MHz. Electric and magnetic fields measured under typical conditions vary from about 200 V/m and 0.1 A/m at 40 cm to about 1000 V/m and 0.35 A/m at 10 cm from the cutting probe lead. These values also vary depending on operating mode. At 16 cm, fields varied from 120 to 1000 V/m and 0.06 to 0.71 A/m depending on the mode of operation. The unit may operate with amplitude modulation at frequencies of approximately 10 to 30 kHz [Ruggera, 1977].

#### HIGH FREQUENCY, 3 MHZ TO 30 MHZ

The HF or shortwave range of frequencies is from 3 to 30 MHz with associated wavelengths of 100 to 10 meters. One characteristic feature of the HF band is long range communication by ionospheric reflection. Because of this propagation characteristic there is always a background of fields from distant sources in the HF band. For example, one set of measurements showed about 50 signals between 0.1 and 1 mV/m from 3 to 30 MHz [Mantiply and Hankin, 1989]. HF is used for long range radio communications for international broadcast by governments and private organizations, amateur radio operators, contract communication providers for aircraft and ships at sea, and military communications. Typical transmitter powers for amateurs are 100 or 1000 watts; professional communication providers use about 10 to 30 kilowatts (kW); and broadcasters operate at 50 to 500 kW. Over-the-horizon (OTH) radar

systems can transmit up to 1200 kW. High frequency sources are also used in industry and medicine for plastic welding and diathermy. Figure 5 summarizes the range of fields measured for several types of HF sources.

#### **Amateur Radio**

Electric and magnetic fields were measured at 9 amateur radio transmitting sites. Fields were determined beneath antennas at a height of 1 to 2 meters for various antenna configurations and frequency bands [Cleveland et al., 1991]. Transmitter powers varied from 100 to 1400 watts for these measurements. The transmitters were set to transmit a constant carrier (no duty cycle correction). The values reported in Table 2 are "example" values. Fields greater than these values were measured in some bands very close to antennas or feed points. Amateur keyed carrier and single-sideband voice transmissions are amplitude modulated at frequencies below 100 Hz. For example, one measurement of an amateur keyed carrier signal resulted in 90 percent modulation from 3 to 100 Hz.

Wavelength Band (meters)	Frequency Range (MHz)	Electric Field Range (V/m)	Magnetic Field Range (mA/m)
80	3.5 - 4.0	1 - 85	4 - 1400
40	7.0 - 7.3	4 - 200	9 - 260
20	14.00 - 14.35	2 - 14	5 - 28
15	21.00 - 21.45	1 - 30	5 - 70
10	28.0 - 29.7	10 - 23	2 - 9

**TABLE 2. HF Amateur Fields Measured at 9 Installations** 

#### Citizen Band Radio

Electric and magnetic fields near several CB antennas have been investigated in some detail [Ruggera, 1979]. Tests were performed with the antennas operating at 27.12 MHz and at 4 watts. Fields were measured as a function of height at a horizontal distance of 5, 12, and 60 cm from the antennas. The maximum electric and magnetic fields measured at 5 cm varied from 230 to 1400 V/m and 0.1 to 1.3 A/m; at 12 cm, from 90 to 610 V/m and 0.05 to 0.8 A/m; at 60 cm, maximum electric fields varied from 18 to 60 V/m and maximum magnetic fields were less than the instrument sensitivity of 0.04 A/m. The CB 40 channel band is from 26.965 to 27.405 MHz. Most transmission is AM, but single side-band can be used.

#### International Broadcast

High power HF transmitters are used for international broadcasts by governments and private organizations. EPA has made measurements at two Voice of America (VOA) sites. VOA typically uses 250 kW transmitters, large rhombic or curtain type antennas, and standard amplitude modulation. Also, 50 kW dual independent side-band transmitters are used for relay. On the Bethany, Ohio VOA station property electric fields of 2.5 to 100 V/m were measured beneath RF transmission lines and rhombic antennas. A study near the VOA transmitter site at Delano, California emphasized measurements of potential exposures in the community of McFarland, 10 km away from the VOA site [Mantiply and Hankin, 1989]. High frequency electric and magnetic fields in McFarland due to VOA were measured



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Fig. 5. High frequency field ranges. The range of fields seen beneath amateur transmitting antennas in a study or 9 installations are tagged by wavelength band; i.e., 80 meter, 40 meter, 20 meter, 15 meter, and 10 meter. Voice of America (VOA) boxes show the range of fields measured on transmitter sites in Bethany, Ohio and Delano, California. The narrow VOA box shows electric fields measured beneath transmission lines and rhombic antennas at Bethany. The wider VOA box shows the range of fields measured 100 to 300 meters in front of rhombic and curtain antennas at Delano. The range of maximum electric and magnetic fields measured 12 cm from several citizen band antennas is labeled CB. The range of operator exposures measured in several studies of heat sealers or dielectric heaters is shown on the right. Finally, the range of exposure fields measured for shortwave diathermy operators is displayed.

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at six sites at 4 frequencies: 6.155, 9.765, 9.815, and 11.74 MHz. For any one frequency, electric field values varied from 1.5 to 64 mV/m, and magnetic fields varied from 0.0055 to 0.16 mA/m. The maximum HF electric and magnetic fields measured just outside the Delano VOA boundary were 8.6 V/m and 29 mA/m.

Electric and magnetic fields were also measured on the VOA Delano site along traverses 1 meter above ground and perpendicular to the direction of propagation in front of a rhombic antenna and a conventional curtain antenna. Fields in front a steerable curtain antenna were investigated by varying its operating direction. All three antennas were operated at 100 kW of input power. At a distance of 200 m in front of the rhombic antenna operating at 9.57 MHz, the electric and magnetic fields varied from 0.45 to 5.0 V/m and 3.0 to 20 mA/m along the traverse. At a distance of 100 m in front of the conventional curtain antenna operating at 9.57 MHz the electric and magnetic fields varied from 4.2 to 9.2 V/m and 18 to 72 mA/m along the traverse. At a distance of 300 m in front of the steerable curtain antenna operating at 5.96 MHz the electric and magnetic fields varied from 1.7 to 6.9 V/m and 14 to 29 mA/m as the antenna was electrically steered to angles of plus or minus 25 degrees from its boresight.

#### **Dielectric Heaters**

Dielectric heaters are used in industry to heat or weld non-conductors such as plastics by applying a strong alternating electric field using metal plates. The range of frequencies can be from a few megahertz to greater than 120 MHz. The most common frequency is 27.12 MHz. Fields measured at the operators position are non-uniform and not well correlated with system power. In 12 studies [Conover et al., 1975; Ruggera, 1977; Hietanen et al., 1979; Conover et al., 1980; Mild, 1980; Stuchly et al., 1980; Aniolczyk, 1981; Cox et al., 1982; Stuchly and Lecuyer, 1985; Joyner and Bangay, 1986; Bini et al., 1986; Conover et al., 1992] field measurements were made at various locations of the operator's anatomy (head, chest, waist) for dielectric heaters operating from 6.5 to 65 MHz. Earlier measurements were made with the operator absent. Measured values of electric and magnetic fields varied from about 20 to 1700 V/m and 0.04 to 14 A/m. Typical values are 250 V/m and 0.75 A/m. These field values are not corrected for duty cycle and do not include values reported as greater or less than the range of a measuring instrument. Reported duty cycles varied from 2.5 % to greater than 50 %. Dielectric heaters are typically on 10 percent of the time. Dielectric heater fields are probably amplitude modulated at multiples of the power frequency.

#### Shortwave Diathermy

Shortwave diathermy is a medical treatment using either continuous or pulsed 27 MHz fields to deep heat a portion of the body. RF power is coupled into the body using either insulated plates or a loop as an applicator. The applicator is connected to an RF power generator using two separate insulated wires. After the applicator is in place the generator is tuned for efficient loading by the body. The plates generate relatively high electric fields to capacitively couple power into the tissue, and the loop generates relatively high magnetic fields to inductively couple power. These fields exist along the leads from the generator as well as at the applicator.

In one study [Kalliomaki et al., 1982] electric and magnetic fields were measured near the patient's body for various types of applicators or electrodes. At the area of treatment electric and magnetic fields varied from 400 to 4000 V/m and 3 to 30 A/m. At areas of the body not prescribed for treatment, fields varied from 20 to 4000 V/m and 0.2 to 14 A/m. Another investigator [Stuchly et al., 1982] found that electric and magnetic fields at untreated areas of the patient ranged from 4 to 2650 V/m and 0.05 to 1.6 A/m.

The dominant source of fields at the operator's position may be the cables. Typical fields near the cables decrease from 2000 to 200 V/m and from 3 to 0.2 A/m as the distance from the cables increases from 5 to 35 cm. Two major studies found similar values for fields at the operators' eyes and waists

[Ruggera, 1980; Stuchly et al., 1982]. The range of fields for the operator was 2 to 315 V/m for the electric field and 0.05 to 0.95 A/m for the magnetic field.

#### VERY-HIGH FREQUENCY, 30 MHZ TO 300 MHZ

The VHF frequency range, from 30 to 300 MHz, has associated wavelengths of 10 to 1 meter. Local broadcast stations including FM and VHF television are common sources at VHF. This frequency range is also popular for two-way voice communications. Figure 6 gives the range of fields and population exposure seen for some VHF sources.

#### FM Radio Broadcast

The median electric field experienced by the urban population in the United States due to FM broadcast at 88 to 108 MHz is about 0.1 V/m with 0.5 percent of the population above 2 V/m [Tell and Mantiply, 1980; Hankin, 1986]. The maximum electric fields at ground level beneath FM towers in the U. S. vary from about 2 to 200 V/m [Gailey and Tell, 1985; U. S. EPA, 1987]. In one case, on a rooftop, the field directly beneath an active antenna at 2 m above the roof was 800 V/m. Measured fields on towers near the antenna vary from 60 to 900 V/m [Tell, 1976; Mild, 1981]; higher electric fields exist within 30 cm of an antenna element. Magnetic fields up to 4.6 A/m have been reported near an element radiating about 300 watts in Sweden [Mild, 1981]. Antenna elements on U. S. towers typically radiate 5 kilowatts.

Fields from FM broadcast are not intentionally amplitude modulated, but transmitter power supply imperfections can cause modulation. In one case, significant 120 Hz AM was seen on an FM signal. Measurements on 10 FM radio stations showed modulation of from 1 to 5 percent from 3 to 100 Hz [Mantiply, 1990].

#### **VHF Television Transmitters**

The VHF television channels are separated into low VHF-TV (channels 2 through 6) at 54 to 88 MHz and high VHF-TV (channels 7 to 13) at 174 to 216 MHz. EPA calculations based on measurements in the late 1970's [Tell and Mantiply, 1980] show that about 16 percent of the population is above 0.1 V/m and 0.1 percent is above 2 V/m due to low VHF-TV. For high VHF-TV, 32 percent of the population was calculated to be above 0.1 V/m and about 0.005 percent above 2 V/m. The maximum fields at ground level beneath VHF-TV towers are estimated to be between 1 and 30 V/m [Gailey and Tell, 1985]. Measured electric and magnetic fields on the tower close to a VHF-TV antenna were 430 V/m and 2 A/m [Mild, 1981].

The television signal consists of an amplitude modulated video signal and an FM audio signal. Amplitude modulation of 4 to 12 percent was measured for 9 TV video signals at 59.94 Hz, the vertical retrace rate.

#### Mobile Transmitters

Electric fields near occupants of cars and trucks with an operating VHF mobile transmitter have been documented [Lambdin, 1979; Adams et al., 1979]. Various vehicles and antenna locations were investigated. Tests made with a 60 watt, 164 MHz FM radio resulted in electric fields ranging from 3.4 to 30 V/m and a 100 watt 41 MHz radio resulted in electric fields from 3.4 to 120 V/m near an occupant. Tests using 100 watt FM radios at 25, 35, 39, 51, and 145 MHz in a midsize automobile resulted in fields from 50 to 150 V/m [Muccioli and Awad, 1987]. The highest electric fields are normally seen near the occupant's head or the driver's hands on the steering wheel. The replacement of metal with plastic and fiberglass in newer vehicles can reduce shielding from the external antenna and increase fields. These fields were measured with the transmitter keyed and no correction for duty cycle.



FREQUENCY

Fig. 6. Range of fields from VHF sources. The lower sections for TV and FM show the upper ranges of general population exposure. The upper box for TV and the middle section for FM show the range of maximum electric field expected on the ground beneath the transmitting antenna. The upper box for FM gives the range of values seen on FM towers close to antenna elements. The range of fields measured in vehicles with a VHF mobile transmitter operating is shown at about 40 MHz. The frequency range of the mobile radios studied is actually 25 to 170 MHz. The maximum electric and magnetic field measured 5 cm form a cordless telephone is shown. The maximum electric field measured 5 cm from a 2 watt hand-held radio is shown as the small box at the upper right.

#### **Portable Transmitters**

Electric and magnetic fields near hand-held transmitters were measured at EPA by searching for the maximum unperturbed field 5 cm from any surface of the unit. The largest fields were typically found near the base of the antenna. The maximum electric and magnetic fields found near a cordless telephone handset operating at 50 MHz were 15 V/m and 18 mA/m. Maximum fields near a 2 watt hand-held radio operating at 164 MHz were 470 V/m and greater than 0.73 A/m - the full scale magnetic field for the instrument.

#### ULTRA-HIGH FREQUENCY, 300 MHZ TO 3 GHZ

The UHF frequency range of 300 MHz to 3 GHz (1 to 0.1 m wavelength) covers UHF television, cellular telephone, many microwave sources and air traffic control radar. Figure 7 gives the range of fields measured for several common UHF sources.

#### **UHF Television Transmitters**

The UHF-TV channels (14 to 67) are in the frequency range of 470 to 806 MHz. General population exposure calculations give about 20 percent of the population above 0.1 V/m and about 0.01 percent above 1 V/m [Tell and Mantiply, 1980]. Maximum fields at ground level beneath UHF-TV towers are estimated to be between 1 and 20 V/m [Gailey and Tell, 1985; Hankin, 1986]. The maximum measured electric field near an antenna element is 620 V/m [Mild, 1981]. The modulation for UHF-TV is the same as for VHF-TV.

#### Cellular Telephones

Cellular base stations transmit in the frequency band of 869 MHz to 894 MHz. Electric fields have been measured at ground level beneath base station towers ranging in height from 46 to 82 m [Petersen and Testagrossa, 1992]. For 1 to 16 channels operating, the maximum fields at ground were 0.1 to 0.8 V/m. Cellular mobile and portable telephones transmit in the frequency range of 824 and 849 MHz. The fields measured inside a car using an external antenna at 3 watts were between 6 and 36 V/m [Balzano et al., 1986]. The maximum fields at 5 cm from a hand-held cellular phone operating at a variable power of 6 to 600 mW are calculated to be from 9.4 to 94 V/m for the electric field and from 41 to 410 mA/m for the magnetic field. The calculation is based on measurements for an 800 mW phone [Balzano, 1984]. Cellular telephones currently use frequency modulation, although future plans call for digital pulse modulation.

#### **Microwave Ovens**

Most microwave ovens operate at 2.45 GHz. Electric fields 1 meter in front of a microwave oven are estimated to range from 0.5 to 7 V/m, with typical values of 1 to 2 V/m. Essentially all field measurements have been made at a distance of 5 cm from the oven [Mild and Lovstrand, 1990]. The 1 meter estimates are based on 5 cm measurements and the field decreasing by 1/r for a point source [Osepchuck, 1979; Reynolds, 1989]. Microwave oven fields vary in time in several ways. The field is pulsed at 60 Hz because of the power supply. Operation of the field stirrer, changes in the load (boiling), and low power, on/off, operation also amplitude modulate microwave oven fields [Mantiply, 1990].

#### **Microwave Diathermy**

Electric fields measured at the operator's location for microwave diathermy system at 2.45 GHz were between 17 and 70 V/m [Ruggera, 1977]. Higher operator exposure was seen for HF diathermy because the longer wavelength fields are more difficult to control.





Fig. 7. Range of fields for UHF sources. The box labeled TV shows the range of exposure for the upper 20 % of the population and the range of fields expected beneath UHF-TV towers. The range of fields seen for cellular hand-held and cellular vehicle antennas overlap. Fields measured on the ground near cellular base station towers are similar to population exposure values due to UHF-TV. The range of fields calculated at one meter from microwave ovens is shown below the measured exposures for operators of medical microwave diathermy equipment. The range of peak and rms electric fields measured close (200 to 600 m) to several air traffic radars at the FAA training center in Oklahoma City and the range of fields from distant radars in the San Francisco area are shown on the right.

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#### **Pulsed Radar**

Conventional pulsed radar emits a microwave pulse, receives a reflected pulse a short time later, and determines the distance to the reflector or target from the time delay. For example, this delay will be about 540 microseconds (round trip time at the speed of light) for a target 50 miles away. The direction to the target is determined from the direction the antenna is pointed in during this process. For a typical air traffic radar, a pulse is transmitted every 1000 microseconds and lasts for about 1 microsecond. The antenna rotates every 5 or 12 seconds and the horizontal width of the beam is about 3 degrees. This implies that the peak field during the pulse while the narrow radar beam is directed at a measurement point is about 400 times the rms field when pulsing and rotation averaging are taken into account. The peak to rms ratio is less in the near field or below the radar where the radar beam is not well defined.

Air traffic radars generally operate at about 1.3 GHz or 2.8 GHz. Measurements at several locations at distances of 200 to 600 m from air traffic radars [Tell and Nelson, 1974a] gave electric fields from 57 mV/m rms or 4.7 V/m peak to 2.5 V/m rms or 960 V/m peak. Measurements for many distant radars operating from 1.3 to 9.5 GHz in the San Francisco area [Tell, 1977] gave rms electric fields ranging from 10 to 64 mV/m and peak electric fields for any one radar of 4 to 14 V/m. Measurements made close to several onboard aircraft weather radars at 9.375 GHz typically showed rms fields ranging from 20 V/m at 10 meters to 200 V/m at 10 cm, see Figure 8. The calculated peak electric field in front of any of these radars was 19 kV/m [Tell and Nelson, 1974b; Tell et al., 1976].

#### SUPER-HIGH FREQUENCY, 3 GHZ TO 30 GHZ

The microwave SHF band from 3 to 30 GHz (wavelength of 10 to 1 cm) includes such sources as terrestrial microwave relay, satellite relay uplinks, aircraft onboard radar (see previous section), and police radar. Figure 8 shows measured fields for some of these sources.

#### **Microwave Relay**

Terrestrial point-to-point microwave radio is typically used to relay telephone conversations and data. The operating frequency varies from 2 to 13 GHz in several bands and electric fields at ground level beneath microwave relay towers are in the range of 20 mV/m to 0.6 V/m [Petersen, 1980; Hankin, 1986]. Systems are being converted from FM to digital pulse modulation.

#### Satcom Uplinks

Fields in the community of Vernon, New Jersey due to large number of satellite uplink transmitters were studied [U.S.EPA, 1986]. In the 6 GHz band fields varied from 70 microvolts/meter to 15 mV/m; in the 14 GHz band, from 0.2 mV/m to 33 mV/m. On a hill in front of one dish operating at a low elevation angle at 6 GHz the electric field varied from 2.4 to 15 V/m.

#### **Police Radar**

The maximum field in the transmitting aperture of police radar units has been evaluated for thousands of devices [Fisher, 1993]. For hand-held 10.5 GHz units the aperture field varied from 33 to 120 V/m; for 24 GHz units the aperture field varied from 27 to 125 V/m. The field for the operator of these units is estimated to be from 1 to 15 V/m if the unit is pointed away from the operator. Fields at a distance of 30 to 300 m in front of these radars varied from about 1 to 0.1 V/m [Hankin, 1976].



Fig. 8. Super-high frequency fields. Fields measured on the ground near terrestrial microwave relay towers are shown at the left. Three boxes show fields measured in Vernon, New Jersey due to satellite uplink antennas. The lower two Vernon boxes show the weak fields measured in the community; the upper box is the range of fields measured on a hill in front of one dish antenna. The aircraft radar line shows fields at 10 cm to 10 m directly in front of the radar. The range of maximum fields measured in the aperture of 10 and 24 GHz police radars are given. Also, the range of fields in the police car to the side of the radar and outside the car in front of the radar (30 to 300 m) are estimated.

#### **DISCUSSION AND CONCLUSIONS**

The exercise of assembling radiofrequency exposure data from so many diverse studies onto a single graph seems useful as a starting point for setting priorities for further study, but may be misleading. Some of the highest fields measured expose very few, if any, people. There is no way to tell from such a presentation how many people are exposed, whether the exposure is whole or partial body, or what the modulation characteristics of the field are. Some attempt has been made in the text to address these issues.

Many sources have never been studied but the range of fields have probably been bracketed. It is unlikely that any high power source of RF exposure has not been included. Comparing in detail the results of studies that have used different protocols, equipment, and judgement in measurement, especially in highly non-uniform near fields, is futile. This points out the need for more standardization in measurement.

Similar studies have not always been done for similar sources; for example, FM antenna fields have been measured close to elements; the same has not been done for TV antenna elements in the United States. Some measurements have been made close to sources while others attempt to determine whole body average exposure; some are made with the exposed person present, but most have been made without a person present.

Intentional transmitting antennas, being engineered to generate fields, are relatively easy to characterize. However, incidental sources such as video displays, microwave ovens, or industrial heaters require significant testing and statistical evaluation to determine exposure. Also, incidental and heating sources have no requirement for modulation control, so modulation (if of interest) must also be tested more extensively. The advent of new low power sources, such as personal communication devices, energy saving lighting, or portable systems that transmit to satellites, places the emphasis for new work on dosimetry and biological evaluation in near fields.

The tendency to be far from high power sources and close to low power sources equivocates setting priorities for exposure assessment based on power or effective radiated power. For example, a simple point source calculation shows that a 10 watt source at 1 meter generates the same power density  $(0.08 \text{ mW/cm}^2)$  as a 100 kW source at 100 meters. In fact, devices not used for telecommunications may generate strong near fields but radiate very little power.

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#### DOSIMETRY OF RADIO FREQUENCY ELECTROMAGNETIC FIELDS\*

Arthur W. Guy\*\*

The first half of the paper provides some of the history of radio frequency (rf) dosimetry, and the latter half discusses some of the new and exciting things that are occurring in the field at the present time. Earlier in this document, Ed Mantiply discussed electromagnetic fields in the environment, so this paper will not discuss what is happening outside of the exposed individual (e.g., see Figure 1).

The most important physical quantity associated with dosimetry is the specific absorption rate of energy (SAR) expressed in units of watts per kilogram (W/kg). Most of the effort in dosimetry is to associate these outside environmental fields E and H and power density with the SAR in the tissues of the exposed body, which is where the cells are located and this is the site of any biological effects if the SAR or the energy that is absorbed is high enough.



Figure 1. Relationship between vf source and dose.

The SAR can be characterized by the simple equation

$$SAR = \sigma E_t^2 \rho^{-1}$$

1

<sup>\*</sup> This paper was updated in March 1995.

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where  $\sigma$  is the electrical conductivity of the tissue,  $E_t$  is the electric field in the tissue, and  $\rho$  is the density of the tissue.

There are several ways to obtain the parameters to solve for SAR in Equation 1. The density and conductivity of the tissue may be measured by various methods. The electric field can be measured directly, or it can be calculated by means of a computer. It's essentially that simple, if you obtain these quantities for any location in the tissues of an exposed subject or laboratory preparation, you can calculate the SAR at that location. The important thing to realize is that the SAR is a function of position. Generally the impact of energy being absorbed by the body is based on what the total body absorption is, that is the energy absorption rate AR which is simply the integration of the SAR over the entire mass, M, of the body given by the equation

$$AR = \int SAR \, dm \qquad 2$$

expressed in watts. This quantity may be expressed in another way as the whole-body-average SAR given by the equation

$$\overline{SAR} = (AR)M^{-1}$$

expressed in units of W/kg. The standards in this country are based on whole-body-average SAR, but we must realize that since energy is absorbed non-uniformly, associated with a given whole-body-average SAR, there are peak SARs that could be 20 or even 100 times greater than the whole-body-average. Generally the safety standards, while based on whole-body average, inherently account for peak SARs.

A simple experimental way for measuring SAR is through temperature change in the exposed tissue of an irradiated subject. This method provides the most accuracy when using a high exposure rate for a short time, thereby depositing the energy in the tissue or exposed subject so fast that the tissue can't dissipate any significant heat during the brief time that the temperature is monitored. Then by noting the short term temperature change,  $\Delta T$ , in degrees celsius, the specific heat of the tissue,  $c_p$ , in kilocalories per kilogram, and the exposure time, t in seconds, one can calculate the SAR by means of the equation

$$SAR = 4186c_{\rm p} \Delta T t^{-1}$$

There are many methods for measuring the temperature change. One approach is direct measurement with a radio transparent probe, such as the Vitek probe invented by Bowman (1976) shown in Figure 2. Care must be exercised in choosing a probe that is truly radio transparent since standard thermocouples and temperature sensing devices have conducting leads connecting the sensor to the instrument. These conducting leads act as receiving antennas that perturb the fields and introduce additional currents or energy-absorption in the tissue where they are imbedded.

An illustration of an example where this probe was used is the small *in vivo* laboratory preparation shown in Figure 3. This was an experiment to establish the SAR related to exposures of chick brain to amplitude modulated rf fields at levels where increased "calcium efflux" rates were reported (Bawin, 1975; Blackman et al., 1980). By exposing the preparations to much higher rf fields than would normally be used for the assessment of biological effects, one can determine the SARs in the tissue associated with different exposure levels in the experimental exposure system. Then based on other means of finding SAR associated with exposures of human beings to rf radiation, information on exposure levels that would produce the same SAR in a human brain, for example, could be obtained.





Figure 3. Example of a radio transparent probe in a small in vivo preparation.

In order to measure the actual electric field in a tissue to determine the SAR by Equation 1, a number of miniature sensing electric field probes have been developed. The operation of one such probe developed by Bassen (1975) is illustrated in Figure 4. The probe consists of a microcircuit antenna with leads leading away from it to appropriate instrumentation calibrated to display the measured field strength. Across that gap of the antenna is a microwave diode, which rectifies the microwave energy to produce a DC current that is conducted through high resistance leads back to a calibrated instrument. The instrument is calibrated to read the electric field strength in volts per meter, or millivolts per meter, in the tissues where the probe is implanted. The complete probe configuration consists of three such dipoles that are orthogonal to each other so that regardless of its orientation, the total electric field in the tissue may be measured by summing its three orthogonal components.

We designed a single element version of a electric field probe to measure the electric field aligned with its dipole axis. We were interested in the energy absorption in the head of a child that might be peering out the back window of an automobile while a cellular telephone was in operation. In order to increase the radiation intensity to a level within the sensitivity of the probe at a distance from the antenna, we used a 10 kilowatt transmitter with a radiation level nearly 10,000 times greater than that of a mobile cellular phone system. To handle this high input power, it was necessary to design a cellular telephone antenna that could handle the power but still have the same radiation pattern as an actual cellular phone antenna. With high level radiation from the antenna, we were able to measure the electric field in the head of the phantom child by aligning the dipole axis of the probe with the electric field at various positions in the head of the child. We were able to characterize the SAR in mW/kg per 1 watt input power to the antenna which was maximum at the surface of the phantom child's face. The absorbed energy was found to drop off very rapidly with distance into the head. The highest SAR was found to be 19 mW/kg at the bridge of the nose of the phantom child.

Measuring electric fields and SAR with a probe in exposed tissue is rather cumbersome and slow, so our laboratory developed more efficient methods for quantifying SAR patterns. By employing a fullscale tissue-equivalent phantom model of man designed to separate along the frontal plane of the body, one can substantially increase the efficiency of quantifying the SAR through the use of thermography. One surface of separation of the split model is first scanned with a thermograph camera to obtain its complete temperature distribution. Then by reassembling the model, exposing it to a radiation source of interest and quickly disassembling it, one can use the thermograph to obtain a new temperature distribution. By subtracting the former temperature distribution from the latter and employing Equation 1, one can calculate the SAR distribution over the frontal plane where the model is split. As an example, the method was employed to determine the frontal plane SAR distribution in a phantom woman model exposed to a 1.5 Tesla General Electric magnetic resonance imaging (MRI) machine. The resulting SAR distribution could be displayed on a computer monitor screen as a map of the SAR pattern as shown in Figure 5. The map is fairly characteristic of SAR patterns obtained both theoretically and experimentally from homogeneous phantom human models exposed to magnetic fields. The configuration of the pattern can be explained by the fact that the eddy currents in the model are maximum at the periphery of the body where they encircle the greatest area that is perpendicular to the time changing magnetic field. When the eddy currents are diverted by sharp nonconducting wedges of air, such as where peripheral parts of the body (arms, legs, neck) join the trunk of the body (axilla, perineum, shoulder) high current densities are produced resulting in the SAR "hot spots" seen in Figure 5. For this case, with the rf magnetic field set for maximum strength, the peak SAR was found to be 7 W/kg, which is slightly less than the IEEE/ANSI allowed peak SAR for the controlled environment (IEEE, 1992). By using a liquid phantom tissue, one can characterize a whole-body-average of SAR by measuring the temperature of the liquid before and after exposure. For such a measurement, one must be very careful to stir the liquid so that the temperature remains uniform while taking the measurements.

Since full-size human models are fairly large and cumbersome to use, for many exposure conditions it is possible to use scale models, typically from one-fifth to one-tenth full scale size to quantify the SAR patterns. Certain conditions must be met in the use of scale models. For example, for a one-fifth






scale model, one has to use five times the full scale exposure frequency, use five times the electrical conductivity of the full scale tissue, and divide the measured SAR by a factor of five to obtain the full scale SAR. The distribution pattern in the scaled model would be the same as in the full scale model except that it is scaled down to the dimensions of the former.

Figure 6 illustrates the SAR patterns obtained thermographically for a scale model man exposed to a magnetic field (Guy et al., 1976). The pattern is very characteristic of the pattern of the full scale woman model exposed to the magnetic fields of the MRI machine.

Calorimetric methods may be used to quantify the whole-body average SAR in animals exposed to rf fields. One common and popular method is through the use of "twin well" calorimeters, as shown in Figure 7. Each device consists of two identical brass cylinders that are insulated from each other with the pair surrounded by, but insulated from, an oval shaped cross-sectional brass cylinder (Guy, 1987). The entire assembly is placed in an insulated box with the oval shaped cylinder held at constant temperature by thermostatically controlled electric or liquid heaters. An array of thermocouples wired in series are attached to the outside wells of the circular metal cylinders. The thermocouples of one cylinder are wired so that the output voltage from the thermocouples are of opposite polarity with that of the other cylinder. Therefore, if the cylinders are at the same temperature, then the output voltage from the entire thermocouple array would be zero since the voltages from the arrays attached to each cylinder would cancel each other. However, if the cylinders were of different temperatures, there would be a differential voltage that would be proportional to the temperature difference.

The calorimeter may be employed in two different ways to measure the whole-body-average SAR in laboratory animals exposed to rf fields. One method would involve drugging the animals to arrest the action of their thermoregulatory systems prior to sham and actual exposures, and the other would involve first sacrificing the animals prior to exposure. This is necessary to allow any increases in body temperature of the exposed animal as compared to a control to be entirely due to the absorbed rf energy rather than from other mechanisms. By placing the animals in the same environmental conditions, except one is under sham exposure conditions and the other exposed to rf fields, the temperature of the latter will rise due to the absorbed rf energy. Each animal is then placed in individual wells of the calorimeter and the wells are sealed with an insulated cap. Since one animal will be slightly warmer than the other, because of the absorbed energy, there will be a voltage output from the thermocouples in the calorimeter until the animals reach the same temperature. The calorimeter may be calibrated by known heat or cold sources so that by integrating the output voltage of the thermocouples over the time it takes the temperatures of the two animals to reach the same value, one can obtain a number that is equal to the total rf energy absorbed by the exposed animal. Dividing this number by the mass of the animal and its exposure time will provide the whole-body-average SAR related to the particular exposure. Thus the SAR for any exposure level can be determined since there is a linear relationship between rf exposure power density and SAR.

In addition to the use of the experimental methods discussed above, there are a number of theoretical models that have been used to obtain induced fields and SAR distributions in animals or humans exposed to rf fields. The first theoretical approach in quantifying the fields and energy absorption in exposed subjects appears to be that of Anne et al., (1961) and his colleagues. These researchers applied the Mie equations, as described by Stratton (1941), to perfect spherical tissue models of various dielectric properties to show how absorption properties changed with exposure frequency and radius of the model. Later investigators (Shapiro, 1971; Ho and Guy, 1975) extended this work to calculate SAR patterns within spheres with layered shells of different tissues. The work demonstrated that the models would resonate at certain frequencies and SAR "hot spots" of much greater magnitude than the surface SAR could occur deep in the model at certain exposure frequencies. The models provided significant insight as to how rf energy is absorbed by exposed subjects at various wavelengths and how at long wavelengths absorption patterns from the electric and magnetic components of the exposure fields could be independently calculated. The studies on spherical models were followed by studies on more sophisticated





Figure 7. "Twin Well" calorimeters for quantifying whole-body average SAR in animals.

two-axis prolate spheroidal models that better represented the bodies of animals and humans (Durney et al., 1975). This work was followed by work on three-axis ellipsoidal models more closely representing the bodies of man and many animals (Massoudi et al., 1977).

Durney et al., (1986) have summarized much of the modelling work in various editions of a U.S. Air Force publication called the Radiofrequency Radiation Dosimetry Handbook which contains SAR data as a function of exposure frequency for every size and shape of subjects ranging from insects to the largest humans. Figure 8 is an example of a typical chart seen in the dosimetry handbook, showing the wholebody-average SAR versus frequency for an average man exposed to a 1 mW/cm<sup>2</sup> radiation field. The upper curve with the highest vertical excursion gives the SAR for E-polarization which corresponds to the case where the electric field is parallel to the long axis of the exposed ellipsoidal subject. We notice that the maximum SAR is approximately 0.25 watts per kilogram which occurs at the so-called resonant frequency near 70 to 80 MHz for an average size man. The SAR falls off fairly rapidly with increasing frequency, approaching an asymptote of approximately 0.03 W/kg at the high frequency end of the spectrum as shown in the figure. The SAR falls off at a rate nearly proportional to the square of the frequency with decreasing frequency below the resonant peak. The term "resonant frequency" is appropriate since the elongated ellipsoidal objects representing man and animals are like radio-receiving antennas. The models absorb the greatest amount of energy when exposed at the resonant frequency. However, if the exposure polarization is changed so that the magnetic field is parallel to the long axis of the ellipsoid, called H-polarization, the SAR versus frequency curve does not have the sharp resonant peak seen for E-polarization. Finally, when the model is exposed with the direction of propagation parallel to the long axis, the polarization is called k-polarization. The curves in Figure 8 indicate that dosimetry associated with human and animal exposure is strongly dependent on the polarization of the exposure fields. As a result of the lack of appreciation of polarization effects on dosimetry by the authors, a number of the older research reports on biological effects of animal exposure leaves one in doubt as to the value of SAR since no polarization information is given with the reported exposure levels.

The simple theoretical models discussed above do not take into account the limbs of the animals and humans nor the realistic irregular tissue boundaries of the subjects that they represent. With the availability of computers and workstations with higher speed and larger memory, there has been a surge of interest in the development of much more realistic models. There have been a number of reports of analysis of SAR distributions in realistic human models exposed to a multitude of different sources using finite difference and finite element types of analyses. These methods essentially divide the tissues of the exposed human or animal subject into small cells or elements with cubicle-, triangular-, or rectangularboundaries. The proper dielectric properties are assigned to each cell based on the tissue type and exposure frequency. Maxwell's equations are than solved numerically on the computer and the average SAR in each cell or element is calculated. At exposure wavelengths that are large compared to the size of the exposed subject, an equivalent electrical circuit can be assigned to each cell and the currents and voltages can be calculated by applying circuit theory to the network created by the combination of the equivalent circuits of each cell. This can be done by using the admittance method based on a nodal analysis as reported by Armitage (1983) or the impedance method using a mesh analysis as reported by Gandhi et al. (1984).

Armitage (1983) applied the admittance method to study the SAR patterns produced in the tissues of patients exposed to magnetic loops and electric sources in connection with the development of rf applicators for producing hyperthermia in the treatment of cancer. Figure 9 illustrates the equivalent circuit used to electrically characterize a cell along with the circuits of its nearest neighbors. Each node is shown as a black dot. The sum of the currents arriving at the node at the center of each cell is equated to zero. Any magnetic field present is going to introduce voltages along each one of the branches between nodes. Any electrode source is going to introduce voltages at the nodes where applied. Trial voltages are placed at each of the other nodes and an iterative technique called "successive over-relaxation" is applied. By using this technique on a high speed computer or workstation, one is able to calculate the current distributions and SAR patterns.



Figure 8. Example of typical chart shown in Radiofrequency Radiation Dosimetry (Durney et al., 1986).

I found the admittance method useful in assessing potential health hazards in the wireless transmission of 60 kilohertz power from a long magnetic wire loop in the floor of passenger airliners to a smaller receiving loops in the seats above to provide electrical power to personal entertainment systems. This wireless transmission of power would allow ground crews to change spacing between different seats to fit different classes of travel without being encumbered by electrical wiring. However, there was concern about potential effects of the magnetic field on the passengers in the aircraft. I felt that the worst case would be when an infant or a child happened to be laying on the floor right on top of the loop, which was designed to be only 1/16th of an inch below the surface of the floor. The worst case also assumed that the front or back of the child was pressed hard against this floor to form a flat surface against the floor. This would never occur in a real situation because of the roundness of the surfaces of the body. In this case, with a 60 kilohertz magnetic exposure field of approximately 380 microtesla ( $\mu$ T) at the surface of the floor, a maximum current density of approximately 180 microamperes per square centimeter ( $\mu$ A/cm<sup>2</sup>) was calculated by the admittance method. A graph of the calculated current distribution is shown in Figure 10.

Orcutt and Gandhi (1988) extended the impedance method using a mesh analysis instead of a nodal analysis to calculate the SAR in man models exposed to low frequency magnetic fields. Gandhi et al., (1984) had reported that the method, with an equivalent circuit of a cell and its nearest neighbors shown in Figure 11, was significantly faster than the admittance method. By summing the voltages



Figure 9. Armitage's admittance method.

around each one of the mesh loops and setting the sum to zero and using the same successive overrelaxation technique as used for the admittance method, Gandhi et al. (1984) were able to calculate the current distribution and SAR patterns in the exposed model.

Both the admittance and impedance methods allow the rapid calculation of current and SAR distributions in complex models consisting of a million or more cells exposed to low frequency fields. Figure 12 illustrates the current density distribution that I calculated by the impedance method for a realistic homogeneous human model exposed to a 1.25  $\mu$ T, 60 Hz magnetic field. The model is based on measurements taken over my own body some years ago in connection with experimental measurements of body impedance. A cell size of a 2.0 x 2.0 cm was used for the calculations. It can clearly be seen that the current distribution pattern is characteristic of the SAR patterns seen in the thermographically derived graphs of Figures 5 and 6 (high levels near the periphery of the body with "hot spots" at the perineum, axilla and shoulders of approximately 1.2 nA/cm<sup>2</sup>).

An advantage in using the admittance and impedance methods is the ease at which it may be applied to complex models composed of different tissue types. Orcutt and Gandhi (1988) used a realistic man model to calculate the induced current distributions in man exposed to low frequency electric and magnetic fields. The model was based on illustrations in an anatomy book of the cross-sectional views of the body of man taken every inch over its entire length in a direction perpendicular to the long axis. Each slice, was divided up into  $1.3 \times 1.3 \text{ cm}$  square cells where the tissue in each cell was identified. A 3-dimensional impedance model with 1.3 cm cubical cells was then assembled by combining all of the



Figure 10. Example of application of the Armitage admittance method.

slices and identifying the dielectric properties of each cubical cell. I used the Orcutt and Gandhi (1988) impedance model to calculate the current distribution for the same exposure conditions used in the homogeneous model, and obtained the results shown in Figure 13. The current distribution pattern is completely different than that shown in Figure 12 for the homogeneous model, as a result of the presence of the tissues of the different organs. One may note, however, that the magnitude is about the same, reaching peak values of approximately  $1.2 \text{ nA/cm}^2$ . The analysis shows that there is now a greater current density at the top center of the body than for the homogeneous model. This is probably due to the interruption of current flow by the air-filled lungs.

The most powerful and popular program currently being used for field and SAR analyses is the finite difference time domain (FDTD) method that directly solves Maxwell's equations in the time domain. The concept was first reported by Yee (1966) at a time when computers were too limited in speed and memory to put it to practical use. With the availability of improved computers, it was finally put to use for the first time nearly a decade later by Taflove and Brodwin (1975a) for solving scattered fields from a dielectric cylinder. This was followed the same year by the first application of the FDTD to calculate the induced fields and temperature in biological media – the human eye exposed to microwave radiation by Taflove and Brodwin (1975b). With Taflove's (1980, 1988) continuing use of the FDTD as an important analytical tool for solving a multitude of different electromagnetic problems, many investigators began to use it (Lau et al., 1986; Sullivan et al., 1987, and 1988) for modelling biological systems exposed to rf fields. The FDTD method has recently become the tool of choice for characterization of the SAR patterns in the human head exposed to cellular telephones.



Figure 11. Gandhi's impedance method.

Gandhi (1995) perfected an FDTD model for calculating the SAR from exposure to RF fields from cellular telephones. His model is based on MRI scans on a human volunteer, obtained every 3 mm from the top of the head to the feet, which provided a resolution of about 2 mm per pixel for each body cross sectional slice. He had the anatomy faculty and their students at the University of Utah identify each tissue in the MRI scan, and code them with numbers. Gandhi and his group identified close to 30 tissues, and assigned each with its own unique dielectric properties. Gandhi then analyzed the SAR patterns with the FDTD method. Figure 14 shows the overall view of one of his scans through the head where the SAR was the greatest, and Figure 15 shows an enlarged view where most of the absorption takes place. We see that most of the energy is absorbed in the ear, where the top of the cellular telephone is placed. Some energy also is absorbed in the brain, but at a much lower level than in the ear. The FDTD technique utilizes as input the construction details, including the RF radiating structure and excitation parameters of the telephone as well as the characteristics and dielectric properties of the exposed body. This information is then fed into a computer and Maxwell's equations are solved using the FDTD method. The result is a detailed 3-dimensional pattern of the electric and magnetic fields and the SAR in the tissue which may easily be visualized by standard graphical visualization software. The highest tissue SARs found in the analysis of eight different cellular telephones approached about 1 W/kg (specifically, 849 mW/kg in the ear), but in the brain itself, the SAR levels were down to 0.3 W/kg or less. These value are consistent with those from the analysis by Balzano (1994) based on actual measurements. Gandhi also did some measurements that confirmed his calculations. On the other hand, Kuster (1994), using the same model as used by Balzano, measured SAR values well over 1 W/kg in the ear and brain tissues when considering the "worst case" exposure situation. However, to obtain these higher values, Kuster placed



Figure 12. Example of application of the Gandhi impedance method (uniform tissue).

the cell telephone antenna at distances much closer to the model head with the microphone further from the mouth (atypical for most cell phone users when talking into the phone) than used by Gandhi and Balzano. He also tested a phone with a shorter one quarter wavelength long antenna (not used in the United States) which results in higher SAR near the base of the antenna. This issue is one that has to be resolved through agreement on antenna types and locations of the antenna relative to the head, typical of cellular telephone use.

With the advent of the higher speed workstations, it looks like FDTD computations as described above can become quite routine. Various laboratories will be able to make use of these techniques to quickly determine the dosimetry relating to exposure from a large number of different types of rf emitters, including MRI scanners, hyperthermia applicators, traffic radar, cellular telephones, handheld police



Figure 13. Example of application of the Gandhi impedance method (3-dimensional tissue).

telephones, and other wireless devices. To give you an idea of how rapidly computer workstation technology is expanding, Digital Equipment Corporation has come out with a series of 64-bit workstations employing the fastest chip in the world. Using the area of the Rose Bowl as an example of the addressable memory and performance of a 32-bit technology workstation, the memory and performance of the new workstations will be equivalent to an area the size of the state of California. With the Cray supercomputers adopting these chips for their new designs and other manufacturers coming out with higher speed and capacity workstations, its not difficult to see how the power of computational methods such as the FDTD will make it an important dosimetry tool in bioelectromagnetics research.







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# **RF SHOCKS AND BURNS: SOME KNOWNS AND UNKNOWNS\***

Om P. Gandhi\*\*

### INTRODUCTION

Even though there is a great deal of data on currents induced in the human body for exposure to radiofrequency (RF) electromagnetic fields both for plane wave, relatively uniform exposures [1-5] and for nonuniform exposures in industrial settings [6-8] for free standing conditions as well as for conditions of contact with energized objects, the data is much more limited on RF shocks and burns [9-11]. This is due to the severity of the phenomenon. From anecdotal stories it is obvious that this can be a serious problem for people exposed to medium and high intensity electromagnetic (EM) fields. Following up on the pioneering work of Dalziel and colleagues [9, 10, 12, 13], Guy and others [14-17] have studied the threshold currents for perception and pain ("let-go") under conditions of continuous rather than intermittent contact with RF energized electrodes. Because of the potential for harm, currents for RF shocks and burns for conditions of intermittent contact were not a part of these studies and thus have not been examined. A limited amount of data is available for transient discharge or conditions of intermittent contact with energized conductors at 60 Hz [18,19]. From the limited data that we will present, it is likely that the stored energy levels needed for RF shocks and burns for transient discharge may diminish with increasing frequency up to 100 kHz, to values that are relatively independent of frequency for frequencies in excess of 100 kHz. Since the absence of data on startle reactions by transient discharges is one of the acknowledged weaknesses of the present day ANSI/IEEE RF safety guidelines [20], it is clear that additional experimental data is needed before this important facet of RF safety is resolved.

### CONTACT HAZARDS IN THE VLF TO HF BAND (10 kHz to 100 MHz)

Ungrounded metallic objects in EM fields develop open-circuit voltages which may be written as:

$$V_{oc} = E_{inc} h_{eff}$$
(1)

where  $V_{oc}$  is the open circuit voltage,  $E_{inc}$  is the magnitude of the incident electric field, assumed to be relatively uniform, and h<sub>eff</sub> is the effective height of the object relative to the ground. Effective height of the object is related to, but is not the same as, the physical height. Effective heights of some commonly encountered objects such as a car, van, bus, fence, metallic roof, etc. have been determined and are given in the literature [14, 17]. Effective height of a car, for example, is about 0.3 m. Effective heights are even larger for bigger or higher objects such as a school bus, metallic roof, etc. For incident electric fields of a few hundred volts per meter, open circuit voltages of tens to hundreds of volts may therefore be created between the object and the ground. Upon touching such an object, a current would flow through the human body whose magnitude will depend on the conditions of contact (contact area, grounding of the body, etc.). Chatterjee, et al. [17] did a study in which the body impedance and threshold currents needed to produce sensations of perception and pain were measured for 367 human subjects (197 males and 170 females of various age groups; 18-35, 36-50 and 51-70 years) for the frequency range 10 kHz to 3 MHz. The study included various types of contact such as finger contact (contact areas 25 and 144 mm<sup>2</sup>) and grasping a rod electrode (diameter = 1.5 cm, length = 14 cm) to simulate the holding of the door handle of a vehicle. The experimental data were used to develop graphs of average threshold incident electric fields that will cause the various sensations such as perception, let-go

<sup>\*</sup> This paper was updated in October 1994.

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(pain), or even burns for adult males and females [17, 21, 22]. Predictions were also made, based on scaling, for the corresponding threshold values for ten-year old children, since the currents for perception and pain were found to be proportional to the (contact area)<sup>1/4</sup>. Taken from reference 17, a representative graph of the threshold incident electric fields for let-go (pain) for grounded adult males and ten-year old children for finger contact (contact area =  $25 \text{ mm}^2$ ) for various vehicles is given in Figure 1. For most of the cases the electric fields are lower than the maximum permissible exposure (MPE) limits given in the ANSI/IEEE C95.1-1992 [20] both for controlled and uncontrolled environments. Given in Figure 2 are the estimated incident electric fields for a wider area grasping contact that will result in currents needed for perception at various frequencies [17]. Average perception currents measured for 197 males for grasping contact with a cylindrical metallic rod of diameter 1.5 cm and length 14 cm (to simulate holding of a handle bar of an automobile) were used to estimate the incident electric fields that will result in such currents for grounded conditions of the subjects. Even though the RF source available at our disposal did not permit us to measure the currents for let-go under grasping contact conditions, we estimate these to be 25 to 30 percent larger than those needed for perception. This would imply that the threshold electric fields needed for let-go for grasping contact conditions would be 25 to 30 percent larger than the values given in Figure 2. From reference 17, perception is one of tingling/pricking sensation at frequencies lower than 70-100 kHz and one of warmth at the higher frequencies. Perception/let-go currents are relatively independent of frequency for frequencies higher than 100 kHz to 50-100 MHz [17, 23].

### SHOCK, FIBRILLATION, AND BURNS

Shock and ventricular fibrillation have been discussed at length in the literature [10, 24-27] for 60 Hz currents. A review of the literature is given in [28]. The values for painful shock and ventricular fibrillation are presented by Dalziel for frequencies up to 10 kHz [13, 26]. It is believed that at higher frequencies, fairly large currents can pass through a human being without causing muscle or nerve stimulation [29]. These currents would, however, produce heating effects in the skin as well as damage to internal organs [25]. Becker et al. [30] and Dobbie [31] have reported values of RF currents which produce burns. Becker et al. [30] claim that 200 mA for 30 seconds produced reddening of the skin of an arm or hand of each of four human subjects, 300 mA for 20 seconds produced pain and blistering, and 400 mA for 10 seconds produced unbearable pain. In each case, the electrode was a 3.8 cm<sup>2</sup> disposable silver ECG electrode. Also, 400 mA through a 1 cm<sup>2</sup> Ferris Red Dot disposable electrode for 20 seconds produced a second-degree burn on the back of a subject's hand. This study was in reference to electrosurgery and so the frequency, though not stated in [30], is assumed to be around 500 kHz. From our results on perception and pain threshold currents beyond about 100 kHz [17], it is expected that the threshold currents for burns at other frequencies would not be any different. Dobbie [31], studying burns during surgical diathermy, reports that 100 mA through a needle electrode used in ECG monitoring over the deltoid muscle causes a unpleasantly hot sensation in 10 seconds. Becker et al. [30] report that 100 mA per square cm of skin for 10 seconds using ECG electrodes produced a burn.

Our measurements of threshold pain current on 197 male subjects indicated that an average current density of approximately 192 mA/cm<sup>2</sup> for contact with the front of the index finger for frequencies greater than or equal to 100 kHz, caused discomfort for a contact area of 25 mm<sup>2</sup>. We believe that this current density would definitely have caused a burn had the subject been told to keep touching the copper plate.

It has previously been mentioned that the threshold current for perception varies with the fourth root of the contact area [17]. It is expected that the threshold current for burns will also follow the same relationship with respect to the contact area, i.e., the current density will vary as  $(area)^{-3/4}$ . For the previously studied contact areas of 144 and 25 mm<sup>2</sup>, the burn thresholds can therefore be obtained by scaling 100 mA/cm<sup>2</sup> needed to cause RF burns [30], according to the relation, burn threshold current density  $\approx$   $(area)^{-3/4}$ . This gives a current density of 76 mA/cm<sup>2</sup> for a contact area of 144 mm<sup>2</sup> and 283 mA/cm<sup>2</sup> for 25 mm<sup>2</sup>.





Average threshold electric field for let-go (pain) for grounded adult males (solid curves) and ten-year old children (dashed curves) in finger contact with various vehicles. Contact area =  $25 \text{ mm}^2$ .

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# Fig. 2.

Average threshold electric field for perception for grounded adult males (solid curves) and ten-year old children (dashed curves) in grasping contact with various vehicles.

The calculated results for threshold E-fields to cause RF burns are plotted in Figures 3 and 4 for male adults and ten-year old children for contact areas of  $25 \text{ mm}^2$  and  $144 \text{ mm}^2$ , respectively. Since the data are not available for children, the threshold fields for children are obtained by scaling the impedance of male adults by the ratio of the height of a standard 50th percentile ten-year old child (1.38m) to the height of a standard 50th percentile male adult (1.75m) and by scaling the burn threshold current for male adults by the square of the ratio of the height of a ten-year old child to the height of a male adult.

### **TRANSIENT DISCHARGES**

A deficiency acknowledged in the ANSI/IEEE C95.1-1992 safety guidelines [20] is that the current limits prescribed for induced and contact currents [Tables 1 and 2, parts B of ref. 20] "may not adequately protect against startle reactions caused by transient discharges when contacting an energized object". In many situations, the hazard of transient discharge may well be the most important issue for safety. Involuntary muscular reactions to transient spark discharges can cause many safety hazards. In our evaluation of construction worker safety at a U.S. Coast Guard Omega Transmitting Station (10.2-13.6 kHz), in collaboration with Robert Curtis (OSHA) and Gene Moss (NIOSH), we found that thresholds of perception, annoyance, and even spark discharges were easily exceeded for intermittent contacts with ungrounded objects (such as cables, metallic tubes, etc.) exposed to RF fields. These, of course, were a result of the energy storage  $(CV_{rms}^2)$  in these objects that could be discharged upon touching or at times even approaching these objects. Another interesting observation was that the perception threshold for finger contact for the Omega site (10.2-13.6 kHz) occurred for stored energy levels on the order of 15-20  $\mu$ J which is considerably lower than 100-150  $\mu$ J (depending on capacitance C of the objects) which is estimated at 60 Hz by experimentation with two subjects [18]. This leads us to believe that the stored energy for perception, annoyance, and spark discharges may be frequency dependent with values being considerably lower at higher frequencies than at 60 Hz where most of the data are presently available. This point of view is also shared by Dr. A. W. Guy [personal communication] who has some unpublished data at 23 kHz and feels that the perception threshold for stored energy may be even lower than 15-20 µJ that we estimate for 10.2-13.6 kHz. In another paper by Delaplace and Reilly [32], data are presented to show that threshold of spark discharge is related to energy (CV<sup>2</sup><sub>rms</sub>) for capacitance less than 575 pF and charge  $(CV_{rms}^2)$  for C > 575 pF. From these limited data, most of which are at 60 Hz, it is obvious that much more data need to be obtained on the stored energy levels for transient spark discharge at various frequencies.

#### CONCLUDING REMARKS

Possibility of RF shocks and burns is a serious problem for personnel working close to high power transmitting antennas in the low, medium, and high frequency bands. Even though a great deal of data is available for threshold perception and let-go currents, the stored energy levels that will result in startle reactions or burns for transient discharges for intermittent contacts are not known. Some limited data points to the possibility that stored capacitive energies needed for transient discharge are likely to decrease with increasing frequencies. Since startle reactions caused by transient discharges may result in accidents, this data and instrumentation to assess which of the objects may pose such a hazard are urgently needed.



Fig. 3.

Threshold E-field for producing burns in adult males (solid curves) and ten-year old children (dashed curves) in finger contact with various vehicles (contact area = 25  $mm^2$ ).

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# Fig. 4.

Threshold E-field for producing burns in adult males (solid curves) and ten-year old children (dashed curves) in finger contact with various vehicles (contact area =  $144 \text{ mm}^2$ ).

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# HUMAN THERMAL RESPONSES TO RF-RADIATION INDUCED HEATING DURING MAGNETIC RESONANCE IMAGING\*

Frank G. Shellock\*\*

## INTRODUCTION

During magnetic resonance imaging (MRI), patients are exposed to a static magnetic field, gradient magnetic fields, and radio-frequency (RF) electromagnetic fields. Each of these forms of electromagnetic radiation can cause unwanted biological effects if applied at sufficiently high exposure levels (1-12). The primary biological effect of exposure to RF radiation is the production of heat that occurs due to resistive losses (1-9). Therefore, the physiologic changes associated with exposure to RF radiation are related to the thermogenic qualities of this electromagnetic field (1, 3-7, 10).

Prior to 1985, there were no published reports concerning the thermal and other physiologic responses of human subjects exposed to RF radiation during MRI. In fact, there has been a general paucity of data obtained in human subjects with respect to their thermal responses to RF radiation. The previous investigations that have been performed in this field have examined thermal sensations or therapeutic applications of diathermy, usually involving only localized regions of the body (2, 8, 9, 13, 14).

Although many studies have been performed using laboratory animals to determine thermoregulatory reactions to tissue heating associated with exposure to RF radiation (2, 8, 9, 15, 16), these experiments do not apply to MRI because the pattern of RF absorption or the coupling of electromagnetic radiation to biological tissues is highly dependent on the organism's size, anatomical factors, the duration of exposure, the sensitivity of the involved tissues, and a myriad of other variables (2, 8, 9, 15, 16). Furthermore, there is no laboratory animal that sufficiently mimics or simulates the thermoregulatory system or responses of man. Therefore, experimental results obtained in laboratory animals cannot be simply "scaled" or extrapolated to predict thermal responses in human subjects exposed to RF radiation (8, 15).

Elaborate mathematic models have been devised to predict "worst case" scenarios of how human subjects may respond to the RF energy that is absorbed during MRI (17-19). A recognized major limitation of modeling, though, is that it is difficult to account for the numerous critical variables (i.e., age, drugs, cardiovascular disease, etc.) that can affect the thermoregulatory responses of human subjects. Most individuals that are exposed to RF radiation during MRI have some underlying health condition or are taking medication that can alter or impair their ability to dissipate heat. More importantly, none of these mathematic models of thermal responses to RF radiation have ever been validated.

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Several investigations have been performed in the recent years that have yielded extremely useful and important data about human thermal responses and other physiologic reactions to RF-radiation induced heating that occurred during MRI (20-34). This article will review and discuss these studies.

## MRI AND THE SPECIFIC ABSORPTION RATE (SAR) OF RF RADIATION

The observed effects that human subjects have to the exposure to RF radiation during MRI are dependent on the amount of energy that is absorbed during the procedure. The term that is used to describe the absorption of RF radiation during MRI is the specific absorption rate, or SAR. The specific absorption rate is the mass normalized rate at which RF power is coupled to biologic tissue and is indicated in units of watts per kilogram, W/kg (20-28, 33, 34). Both peak and whole-body averaged SARs are used to characterize the relative amounts of RF radiation that an individual encounters during an MRI examination.

Measurements or estimates of SAR are not trivial, particularly in human subjects, and there are several methods of determining this parameter for the purpose of RF energy dosimetry during MRI (20, 28, 34-38). The SAR that is produced during MRI is a complex function of numerous variables including the frequency (which, in turn, is determined by the static magnetic field strength), the type of RF pulse used (i.e.,  $90^{\circ}$  or  $180^{\circ}$ ), the repetition time, the pulse width, the type of RF coil used (i.e., send/receive body coil or send/receive surface coil), the volume of tissue contained within the coil, the resistivity of the tissue, the configuration of the anatomical region exposed, the orientation of the body to the field vectors, as well as other important factors (1, 3-7, 37, 38).

The efficiency and absorption pattern of RF energy are mainly determined by the physical dimensions of the tissue in relation to the incident wavelength (2, 8, 9). Therefore, if the tissue size is large relative to the wavelength, energy is predominantly absorbed on the surface; if is it small relative to the wavelength, there is little absorption of RF power (2, 8, 9).

During MRI, tissue heating results primarily from magnetic induction with a negligible contribution from the electric fields (37, 38), so ohmic heating is greatest at the surface of the body and is minimal at the center of the body; see Figure 1. Predictive calculations and measurements obtained in phantoms and in human subjects exposed to MRI support this pattern of temperature distribution (2, 8, 9, 37, 38).

## **RECOMMENDED SAFE LEVELS OF EXPOSURE TO RF RADIATION DURING MRI**

The Food and Drug Administration (FDA) is responsible for providing guidelines and recommendations for the safe use of MRI systems in the United States. On July 28, 1988, MRI systems were reclassified from class III, in which premarket approval is required, to class II, which is regulated by performance standards, as long as the MRI system is within the "umbrella" of defined limits addressed below (53). Subsequent to this reclassification, new MRI systems had only to demonstrate that they were "substantially equivalent" to any class II device that was brought to market using the premarket notification process (510[k]) or, alternatively, to any of the devices described by the various MR system manufacturers that had petitioned the FDA for such a reclassification.

At the present time, the safe levels for exposure to RF radiation during MR procedures recommended by the FDA provide two options to control the risk of systemic thermal overload and local thermal injury. Either SAR levels or temperature criteria may be adhered to, as follows (53):

(1) The exposure to RF energy below the level of concern is an SAR of 0.4 W/kg or less averaged over the body, and 8.0 W/kg or less spatial peak in any 1 gram of tissue, and 3.2 W/kg or less averaged over the head; or



- Fig 1. MRI was performed on a spherical, seedless watermelon (diameter 24 cm) to study the depth of heating. Thermistor needles were inserted into the watermelon before (opened square) and after MRI performed with a 1.5 Tesla/64 MHz MRI scanner using a quadratrue body coil at whole-body averaged SARs of 1 W/kg (closed circle) and 2.5 W/kg (opened circle) for 30 min. Room temperature was 20.5°C and relative humidity was 45%. The temperature plot shows that there is predominantly peripheral heating with relatively small temperature changes in the central part of the watermelon that occur during MRI performed at 1.5 Tesla/64 MHz.
  - (2) The exposure to RF energy that is insufficient to produce a core temperature increase of 1°C and localized heating to no greater than 38°C in the head, 39°C in the trunk, and 40°C in the extremities, except for patients with impaired systemic blood flow and/or perspiration (i.e., patients with compromised thermoregulatory systems).

Furthermore, the above exposure levels apply to normal clinical environments where the individual is resting and lightly dressed. The exposures to RF radiation during MRI procedures must be below either of the above two levels of concern by presentation of valid scientific measurement or calculational evidence sufficient to demonstrate that RF heating effects are of no concern (53).

# ASSESSMENT OF THERMAL AND OTHER PHYSIOLOGIC RESPONSES TO RF RADIATION INDUCED HEATING DURING MRI

Obtaining thermal and other physiologic measurements in human subjects within the harsh electromagnetic environment of MRI is not a simple task. The high-field strength static magnetic fields can create missiles out of monitors, which typically contain ferromagnetic components (12, 39, 40). In addition, the static, gradient, and RF electromagnetic fields may adversely interfere with the proper operation of the monitoring equipment (39, 40). In turn, the monitors, themselves, may produce subtle or significant imaging artifacts during operation by generating "RF noise" that can significantly distort the quality of MR images (12, 39, 40). In consideration of the above, monitors must be specially adapted or modified and then rigorously tested prior to use in the MRI environment.

Currently, there are a variety of MRI-compatible monitors, as well as other patient support devices that are commercially available (39-42). Every physiologic parameter that is obtainable under normal

circumstances in the critical care area or operating room may be recorded during MRI, including heart rate, oxygen saturation, end-tidal carbon dioxide, respiratory rate, blood pressure, cutaneous blood flow, and temperature (39-42).

For assessment of thermal response during MRI, volunteer subjects or patients have been continuously or semi-continuously monitored throughout the experimental procedures using several different types of devices (20, 22-27, 31-34). For example, sublingual pocket or tympanic membrane temperature (note that there is a good relationship between sublingual pocket temperature or tympanic and esophageal temperatures (43)) were typically obtained immediately before and after MRI using sensitive electronic thermometry or infrared devices (20, 23, 26). Skin temperatures were measured immediately before and after MRI procedures with a highly accurate infrared thermometer or thermographic equipment (20, 22, 30, 34, 44). Body and skin temperatures measured at multiple sites were recorded before, during, and after MRI with a fluoroptic thermometry system that is unperturbed by electromagnetic radiation (34, 42). Heart rate, oxygen saturation, blood pressure, respiratory rate, and cutaneous blood flow, which are important physiologic variables that change in response to a thermal load, were typically monitored before, during, and after MRI to assess the thermoregulatory system reaction of human subjects exposed to RF radiation-induced heating (12, 20-27, 40). All of these parameters were obtained with MRI-compatible devices that have been extensively tested and demonstrated to provide sensitive and accurate data; see Figure 2.

# THERMAL AND OTHER PHYSIOLOGIC RESPONSES TO RF RADIATION INDUCED HEATING DURING MRI

The increase in tissue temperature caused by exposure to RF energy during MRI depends on multiple physiologic, physical, and environmental factors including the duration of exposure, the rate at which energy is deposited, the ambient temperature, humidity, and airflow over and around the patient within the MRI system, the status of the patients thermoregulatory system, and the amount of insulating clothing on or over the patient.

Although the primary cause of tissue heating during MRI procedures is attributed solely to RF radiation, it should be noted that various reports have suggested that exposure to static magnetic fields used for MRI may also cause temperature changes (45, 46). The mechanism(s) responsible for such an effect remains unclear, but the results of these studies have warranted investigations in human subjects to determine if there is any contribution of the static magnetic field to the temperature changes that may be observed during MRI. Therefore, studies were conducted in human subjects exposed to a 1.5 Tesla static magnetic field in order to determine if there were any changes in body and/or skin temperatures (31, 32). The data revealed that there were no statistically significant alterations observed in any of the recorded physiologic parameters (31, 32); see Figure 3. Tenforde (47) examined this phenomenon, as well, in laboratory animals exposed to static magnetic fields of as high as 7.55 T and also reported no effect. As far as the potential for production of heat by gradient magnetic fields is concerned, this is not believed to occur with the use of the conventional pulse sequences used for clinical MRI procedures (37, 38).

The first study of human thermal responses to RF radiation induced heating during MRI was conducted by Schaefer et al. (25). Temperature changes and other physiologic alterations were assessed in volunteer subjects exposed to relatively high whole-body averaged SARs (i.e., approximately 4.0 W/kg). The recorded data indicated that there were no excessive temperature elevations or other deleterious physiologic consequences related to this exposure to RF radiation (25).

Several studies were subsequently conducted involving volunteer subjects and patients undergoing clinical MRI procedures with the intent of obtaining information that would be applicable to the patient population typically encountered in the MRI setting (20-28, 30, 33, 34). The whole-body averaged SARs ranged from approximately 0.05 W/kg (i.e., for MRI procedures involving imaging with a transmit/receive



Fig 2(a). MRI-compatible respiratory monitor.



Fig 2(b). Heart rate and blood pressure monitor.



Fig 2(c). Cutaneous blood flow monitor.



Fig 2(d). Multi-probe, fluoroptic thermometer.



Fig 2(e). Fiber-optic pulse oximeter



Fig 3. Esophageal temperature measured in 11 human subjects during a 20 minute exposure to a 1.5 Tesla static magnetic field. There were no statistically significant changes in temperature caused by exposure to the static magnetic field.

head coil) to 4.0 W/kg (i.e., for MRI procedures involving the imaging of the spine or abdomen with a transmit/receive body coil) (20-28, 30, 33, 34). These studies demonstrated that changes in body temperatures were relatively minor (i.e., less than 0.6°C) (20-28, 30, 33, 34); see Figures 4 to 8. There tended to be statistically significant increases in skin temperatures that were also of no meaningful physiologic consequence (20-28, 30, 33, 34). Furthermore, there were no associated deleterious alterations in any of the hemodynamic parameters that were assessed during these investigations (i.e., heart rate, blood pressure, and cutaneous blood flow) (20, 23, 26) (Figure 7).

Of further note is that there was a poor correlation between body or skin temperature changes versus whole-body averaged SARs during clinical MRI (Figure 4). This is not unusual considering all of the variables that may alter thermoregulation in a patient population (48-52). Therefore, the thermal response to a given SAR may be quite variable depending on the individual's own thermoregulatory system and the presence of one or more underlying condition(s) that may alter or impair the ability to dissipate heat (4-7). An extensive thermophysiology investigation using multiple fluoroptic thermometry probes that are unperturbed by electromagnetic fields (34) demonstrated that human subjects with normal thermoregulatory systems exposed to MRI at whole body averaged SAR levels up to 4.0 W/kg (i.e., ten times higher than the level currently recommended by the United States Food and Drug Administration (53)) had no statistically significant increases in body temperatures and have statistically significant elevations in skin temperatures that were not excessive (Figure 8). The results of this study suggested that the recommended exposure to RF radiation during MRI for patients with normal thermoregulatory function may be too conservative (34).

Research has been conducted in volunteers exposed to MRI performed at a whole body averaged SAR of 6.0 W/kg in cool (22.5°C) and warm (33°C) environments in order to characterize thermal and other physiologic responses to this high exposure to RF energy since some of the newly developed pulse sequences have potentially high SARs associated with their use (54-56). Tympanic membrane temperature, six skin temperatures, heart rate, blood pressure, oxygen saturation, and skin blood flow were monitored before, during, and after exposure to the RF energy; see Figure 9. In the cool environment, there were statistically significant increases in tympanic membrane, abdomen, upperarm, hand, and thigh temperatures as well as heart rate and skin blood flow. In the warm environment, there were statistically significant increases in tympanic membrane, hand, and chest temperatures as well as systolic blood pressure and heart rate. Each of the temperature increases were within FDA guidelines (53). These data indicate that MRI performed at 6.0 W/kg can be physiologically tolerated by individuals with normal thermoregulatory function (54).

Of additional note is that the subjects' perception of tissue heating was greater when the subjects underwent MRI at an SAR of 6.0 W/kg in the cool environment compared with their experience in the warm environment. This indicates that it would not be useful to pre-cool subjects that will subsequently undergo high SAR procedures in order to enable them to better tolerate these procedures, as has been suggested by some researchers and manufacturers of MRI systems.

Additional studies are presently needed in order to assess thermal responses of patients with conditions that may impair their ability to dissipate heat (e.g., elderly patients; patients with underlying diseases, or obesity; and patients taking medications that affect thermoregulation, such as calcium blockers, beta blockers, diuretics, vasodilators, sedatives, anesthetics, etc.) (48-52) before subjecting them to MRI procedures that require high SARs. There is currently an on-going effort to characterize the thermal and other physiologic responses of these patient groups to RF radiation induced heating during MRI examinations that require high SARs.





Change in body temperature versus exposure to whole-body average SAR's during clinical MRI procedures. Note that there is a poor correlation between these two variables.



Fig 4(b).

Change in skin temperature versus exposure to whole-body averaged sar's during clinical MRI procedures. Note that there is poor correlation between these two variables.



Fig 5. Sublingual pocket temperature, forehead skin temperature, ear skin temperature, and ear skin blood flow measured immediately before and after clinical MRI procedures involving the patients head. There were statistically significant increases (p < 0.01) in sublingual pocket, forehead skin, and ear skin temperatures and in ear skin blood flow (see reference 23).



Fig 6. Average body (sublingual pocket) and skin temperatures measured immediately before and after MRI of the brain at 1.5 T/64 MHz using a head coil (N=35). There were statistically significant increases in forehead and skin and outer canthus skin temperatures (see reference 26).



Fig 7. Average heart rate and systolic and diastolic blood pressures immediately before and after MRI of the brain at 1.5 T/64 MHz using a head coil (N-35). There were statistically significant decreases in each of these measured parameters (see reference 26).



Fig 8. Sublingual and multiple skin temperatures measured at 1-min intervals with a fluoroptic thermometry system (Luxtron) before (baseline), during (MR imaging), and after (post-MR imaging) MRI performed at wholebody averaged SAR of 2.8 W/kg. Note that there was little or no change in sublingual or body temperature, whereas there were slight to moderate changes in skin temperatures (depending on the site of the measurement) during MRI. After MRI, some skin temperatures returned to the baseline level, whereas others remained elevated during the 20-min post-MRI evaluation period (see reference 34).


Fig 9(a). Changes in tympanic membrane, abdomen, forehead, upper arm, hand, chest, thigh, and calf skin temperatures associated with MRI performed (N = 6 volunteers) at a whole body averaged SAR of 6.0 W/kg in cool and warm environments (see reference 54).



Fig 9(b).

Changes in systolic blood pressure, diastolic blood pressure, mean blood pressure, heart rate, oxygen saturation and cutaneous blood flow associated with MRI performed (N = 6 volunteers) at a whole body averaged SAR of 6.0 W/kg in cool and warm environments (see reference 54).

## MRI AND TEMPERATURE-SENSITIVE ORGANS: THE TESTIS AND EYE

Certain human organs that have reduced capabilities for heat dissipation, such as the testis and eye, are particularly sensitive to elevated temperatures. Therefore, these are primary sites of potentially harmful effects if RF radiation exposures during MRI are excessive.

For example, laboratory investigations have demonstrated detrimental effects of testicular function (i.e., a reduction or cessation of spermatogenesis, impaired sperm motility, degeneration of seminiferous tubules, etc.) caused by RF radiation-induced heating from exposures sufficient enough to raise scrotal and/or testicular tissue temperatures between 38 to  $42^{\circ}$ C (57).

Scrotal skin temperatures (which are an index of intratesticular temperatures because a high correlation has been demonstrated between intratesticular and scrotal skin temperatures) (58) were measured in volunteer subjects undergoing MRI at a whole-body averaged SAR of 1.1 W/kg (27). The largest change in scrotal skin temperature was 2.1°C and the highest scrotal skin temperature recorded was 34.2°C (27). These temperature changes were below the threshold known to impair testicular function (57). However, inordinately heating the scrotum during MRI could exacerbate certain pre-existing disorders associated with increased scrotal/testicular temperatures (e.g., acute febrile illnesses, varicocele, etc.) in patients who are already oligospermic and could lead to temporary or permanent sterility. Therefore, additional studies designed to investigate these issues are needed, particularly if patients are scanned at whole-body averaged SARs higher than those previously evaluated (which is entirely possible; since there is a trend to use newly developed pulse sequences that have associated high SARs to image the scrotum).

Dissipation of heat from the eye is a slow and inefficient process due to its relative lack of vascularization. Acute near-field exposures of RF radiation to the eyes or heads of laboratory animals have been demonstrated to be cataractogenic as a result of the thermal disruption of ocular tissues if the exposure is of a sufficient intensity and duration (59). An investigation conducted by Sacks et al. (60) revealed that there were no discernible effects on the eyes of rats produced by MRI at exposures that far exceeded typical clinical imaging levels. However, as previously indicated, it may not be acceptable to extrapolate these data to human subjects considering the coupling of RF radiation to the anatomy and the tissue volume of laboratory rat eyes compared to those of humans.

Corneal temperatures (corneal temperature is a representative site of the average temperature of the human eye) (61) have been measured in patients undergoing MRI of the brain using a send/receive head coil at local SARs up to 3.1 W/kg (24). The largest corneal temperature change was 1.8°C and the highest temperature measured was 34.4°C. A more recent study (33) examined corneal temperatures in patients with suspected ocular pathology who underwent MRI using a special eye coil; again, there were no excessive corneal temperature elevations. Because the temperature threshold for RF radiation-induced cataractogenisis in animal models has been demonstrated to be between 41 to 55°C for acute near-field exposures, it does not appear that clinical MRI using a head coil or an eye coil has the potential to cause thermal damage in ocular tissue. The effect of MRI performed using higher SARs and the long-term effects of MRI on ocular tissue remains to be determined.

## **MRI AND "HOT SPOTS"**

Theoretically, RF radiation "hot spots" caused by an uneven distribution of RF power may arise whenever current concentrations are produced in association with restrictive conductive patterns. There has been the suggestion that RF radiation "hot spots" may occur during MRI and generate thermal "hot spots" under certain conditions. Because RF radiation is mainly absorbed by peripheral tissues, thermography has been used to study the heating pattern associated with MRI at high whole-body averaged SARs (22, 30). This research demonstrated that there was no evidence of surface thermal "hot spots" related to performing MRI in human subjects. The thermoregulatory system apparently responds

to the heat challenge induced by RF radiation by distributing the thermal load, producing a "smearing" effect of the surface temperatures; see Figure 10. However, there is a possibility that internal thermal "hot spots" may develop during MRI. This issue is currently undergoing investigation in human subjects.

A report by Shuman et al. (35) indicated that significant temperature rises occur in internal organs produced during MRI performed in laboratory dogs. This study was conducted on anesthetized animals and is unlikely to be pertinent to conscious adult human subjects because of the previously discussed factors relating to the physical dimensions as well as to the dissimilar thermoregulatory systems of these two species. However, these data may have important implications for the use of MRI in pediatric patients because this patient population is typically sedated or anesthetized for MRI examinations and the physical dimensions of the dog are comparable to those of the pediatric population that frequently is examined by MRI. Obviously, research is required to examine this issue more closely.

# FUTURE STUDIES OF THERMAL RESPONSES TO RF-RADIATION INDUCED HEATING DURING MRI

Recent advances in MRI have produced special pulse sequences (i.e. RARE, fast spin echo, etc.) that allow imaging to be performed five to ten times faster than previously possible (56). This requires a substantial increase in RF power that is predicted, in some cases, to exceed a whole-body averaged SAR of 10 W/kg (D.J. Schaefer, General Electric Company, personal communication, 1991). Both the clinical importance and the cost-effective use of MRI accomplished with these new pulse sequences are obvious. However, the safety of subjecting patients to RF energy at these potentially excessive levels is unknown. Therefore, studies are currently examining the human thermoregulatory responses to SARs that are even higher than those that have been studied in recent years (54). As previously indicated, preliminary results of these investigations are encouraging with respect to the ability of individuals with normal thermoregulatory function to tolerate MRI examinations with high SARs.

In addition, there are now whole-body MRI systems with a static magnetic field strength of 4.0-T that are being used for a combination of imaging and spectroscopy on human subjects (62, 63). Imaging at 4.0-T uses approximately seven times as much RF energy as a 1.5-T MRI scanner (62). Investigations evaluating thermal responses in human subjects will also be needed to assess the safety of these powerful MRI devices.

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Fig 10. Thermographs obtained from the back of a human subject before (top) and after (bottom) a 45-min procedure performed on the abdomen with a 1.5-T/64-MHz MRI scanner at a whole-body average SAR of 3.2 W/kg. There was no evidence of any surface "hot spots" or of excessive temperature elevations. The thermoregulatory system produced a "smearing" effect such that the increased surface temperatures after MRI were evenly distributed (see references 22 and 30).



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# EPIDEMIOLOGIC STUDIES OF NON-IONIZING RADIOFREQUENCY EXPOSURES\*

Genevieve Matanoski\*\*

This paper discusses several epidemiology studies on the potential risks of radiofrequency (RF) exposures. The studies in the literature have little information on the details of exposures to the population. Few studies include large populations from which we could gain information on human responses to RF. In fact, the RF exposed workers are often a subset of a larger population exposed to non-ionizing radiation. Despite these limitations, we will review the few studies in the recent literature in an attempt to determine whether there are any chronic effects from RF exposures.

For ease of discussion, the studies have been divided into groups. The first group will be cohort studies that looked at electromagnetic (EM) fields in general. Within these studies (see Table 1), specific jobs which may have resulted in RF exposures, such as electronics, can be selected for review. However, these job titles are nonspecific in regard to actual exposures to RF. The studies by Vagero (1983, 1985) and by DeGuire (1988) demonstrate a positive risk for melanoma of the skin in individuals who are in the telecommunications and electronics industries. However, the studies do not indicate which jobs may have been related to the risks. However, in each of the studies, the relative risks were significant and the values ranged from levels of 1.5 to about 2.5. These studies did not report excess risks of brain cancers or leukemia, which are often reported in studies of electrical workers. These are the only studies reporting excesses of melanomas. However, this does not mean that the other studies are necessarily negative; many studies never looked for melanoma as an outcome.

McLaughlin (1987) looked at only leukemia risks in association with electrical jobs and found no excess risk in electricians, powerline workers, or telecommunications employees. Lin (1989) investigated the risks of brain tumors in the telecommunications industry and found no association between leukemia and work in the industry; however, he did find an association with brain cancers based on a very small number of cases. Again, both studies use a non-specific characterization of the telecommunications industry and do not designate jobs or exposures.

A study of Navy personnel by Garland (1990) only reported on leukemia risks. Although no other risks were reported, authors usually examine other diseases in any cohort study to see if anything else appears to be occurring in excess. The personnel jobs were broken down into three groupings: radio men, electronics technicians, and electricians' mates. The only group at risk was the electricians, not the radio men or the electronics technicians.

Törnqvist (1991) studied the jobs of Swedish workers with leukemia and brain cancers and compared the risk of electrical and electronics workers to all other workers. The group of tele-radio and TV repair technicians who might be suspected of having RF exposures showed no significantly elevated standard mortality ratios (SMRs). He reports a very small excess risk of leukemia when he puts all electric work into one group which includes engineers and technicians. In general, he has found no risk for either leukemia or brain tumors in the group who might be exposed to RF non-ionizing radiation. However, both SMRs just exceeded 1.0.

<sup>\*</sup> This paper was updated in October 1994.

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Author	Subjects/Exposure	Risks
Vagero 1985	Telecommunications Industry	Melanoma 2.5*Sig. No/xs brain, leukemia
Vagero 1983	Electronics Industry	Melanoma 1.35*Sig. No/xs brain, leukemia
McLaughlin 1987	Electricians Powerline workers Telecommunications	Only leukemia reported 0.8 (42 cases) 1.0 (13) 1.1 (13)
DeGuire 1988	Telecommunications	Melanoma 2.7*Sig. (10) [No other cancer reported]
Lin 1989	Telecommunications	All cancers 1.01 (129) Brain cancer 2.4 (5) [No other cancer reported]
Garland 1990	Navy Personnel Electricians' mates Electronics technicians Radiomen	Only leukemia reported 2.4*Sig. (7) 1.1 (5) 1.1 (4)
Hutchinson 1991	All electric Telegraph, radio, radar operators Electronics technicians Television, radio repairmen Radio, radar mechanics	Summary of all data on leukemia Cl, 95% 1.19 (1.12, 1.26) 1.59 (1.29, 1.96) 1.18 (0.75, 1.88) 2.24 (1.37, 3.66) 0.47 (0.18, 1.26)
Törnqvist 1991	All Swedish workers All elec./electronic engineers and technicians Tele-radio TV repair	Leukemia         Brain           SMR         95%, Cl         SMR         95%, Cl           1.3         (1.0, 1.7)         0.9         (0.7, 1.3)           1.1         (0.6, 1.8)         1.2         (0.7, 2.0)

 Table 1. General Studies: Electrical Workers Exposed to RF Radiation

Hutchinson (1991) reported a summary or meta-analysis of all the studies on leukemia and possible exposures to EM fields. The summary focused on leukemia as reported in al studies done to that date. He examined the risks in the various subsets of occupations within the studies. The overall group showed about a 1.2-fold excess risk of leukemia for all individuals who worked anywhere in the electrical/electronics industry. For the total group, there was a significant difference in risk. He has examined telegraph radio/radar operators as a subgroup in these combined studies. There is a significant excess of risk of 1.6 in this group of workers. In addition, television and radio repairmen have a significant excess risk of 2.24. The telecommunications industry and electronics industry as a whole showed no excess risk of leukemia. Essentially, compiling all of the studies on leukemia, there is a significant excess risk for the radar and radio operators, and for television repairmen. The jobs of radio repairmen and radio mechanics show conflicting results in two subgroups which include these workers.

These general studies of cohorts of workers who are assumed to have RF exposures have shown some excesses of leukemia; however, there are inconsistencies across the studies and there is no information on the actual exposures in these jobs. From Hutchinson's meta-analysis, the excess risk of leukemia may be associated with work as a radio or radar operator. Only one cohort study examined the association between brain tumors and radiofrequency exposures and three cohort studies examined the association with melanoma. Brain tumor and work in jobs with possible RF exposures was not significant in the one study, while melanoma were significantly associated with work in the telecommunications industry in three studies. No studies actually associated the cancers with exposures to RF radiation in these jobs.

Table 2 presents case-control studies of brain cancers. These studies compare the occupations of individuals with brain cancer to those of people with no brain cancer. The cases are often identified from a cancer registry, hospital records, or deaths. In these studies, occupations are often identified from death certificates or hospital records. The best studies seek information on occupations from the patient or the next of kin. The investigators try to determine the type of work performed by the cases and controls and try to characterize that work in detail. The problem the investigators have is that cases of brain cancer are usually deceased, but the controls are living. Thus, the quality of the data between cases and controls differs.

Author	Subjects/Exposure	Risks
Lin 1985	Glioma/astrocytoma deaths 519 Controls: non-cancer deaths 519 Occupation on death certificate Panel rating exposures: by job	Definite EM 2.15 (1.10, 4.06) Probable EM 1.95 (0.94, 3.91) Max. risk: electric and electronics engineers 18 cases/6 controls among gliomas
Thomas 1987	<ul><li>435 brain cancer</li><li>386 other deaths as controls</li><li>Occupation: next-of-kin</li><li>Panel rating exposures</li><li>No control other occ. materials</li></ul>	MW/RF Expos.1.6(1.0, 2.4)MW/RF Expos. in elec.or electronics2.3Exposed but never inelec. or electronics1.0(0.5, 1.9)Dose response by duration worked inMW/RF exposureAstrocytomas higher 4.6(1.9, 12.2)
Savitz 1989	1,095 brain cancer in 16 U.S. states Occupation on death cert.	Electric workers 1.5 (1.02, 2) Elec. and electronic tech 3.1 Elec. power repair 2.4
Brownson 1990	Cancer registry 312 WM brain 1,248 other cancers Occupation on hospital record	Communication workers 1.4 (0.5, 4.1) Utilities and sanitation services 0.5 (0.1, 1.7)

## Table 2. General Studies: Brain Cancer

Several case-controls studies are presented. One is a study by Lin (1985) which examined deaths from brain cancers and non-cancer deaths in Maryland and compared each individual's occupation as listed on a death certificate. A panel then examined those jobs and judged whether the jobs on the list exposed individuals to various types of EM fields. The first group consisted of electricians, electrical engineers, and other electrical poweer workers. The second group consisted of electronics engineers and others primarily exposed to RF waves. The number of cases was large, 579. Lin reported a significant difference in risk for those who were likely to be highly exposed to electric fields. He showed a somewhat lesser risk for those who has "probable" EM exposures and for a group of electronics engineers

who may have had RF exposures. The maximum risk was for electronics engineer: almost three-fold for gliomas. This particular study offers little information in regard to pure RF or microwave exposures.

Thomas (1987) used a similar case-control study of brain cancer deaths and other death controls in three states. The author examined the occupations of cases and controls through interviews with the next of kin. This allowed comparison of total occupational histories. Although this information is somewhat limited since next of kin may not know exactly what work an individual performed, this, in general, is a better study than the one previously described. A panel rated the exposures relating to each job to determine which jobs were likely to have had microwave or RF exposures. Thomas was specific about the exposures of interest. Individuals whose jobs exposed them to microwaves and RF radiation had a significant excess risk of brain tumors with an odds ratio of 1.6. The odds ratio was higher (2.3) and still significantly increased in those who worked in electronics or electrical jobs and were exposed to RF or microwave radiation. Those who were exposed but never worked in the electronics and electrical industry had no excess risk. Thus, it would appear that exposure to microwaves and RF waves, which was associated with brain cancer in this study, was strictly in individuals exposed and working in the electronics industry. There was a positive dose-response relationship with increasing risk of brain cancer, associated with increasing duration of work with microwave and RF radiation exposures. The odds ratio was increased to 4.6 when the exposure was associated with a specific brain tumor, astrocytomas. The study by Thomas is one of the stronger studies in terms of design and exposure estimation. The study still does not identify exactly what exposure, and at what level, RF or microwave radiation is associated with brain cancer. This study does correct for smoking, but does not correct for other materials that might have been present in the occupational setting.

There are two other case-control studies of brain tumors. Loomis and Savitz (1989) examined the risk of brain cancer using the occupations as listed on death certificates. The occupation on the death certificate supposedly represents the "usually occupation", but the information often is given by a respondent at time of death or is taken from a hospital record. If someone has had two or three jobs, the most recent occupation is usually listed on the death certificate. This death certificate occupation has limited value in identifying exposures compared to taking a complete work history as done by Thomas. Exposures to non-ionizing radiation were based on job title. The Loomis and Savitz study showed an apparent increased risk of brain cancers for electrical workers in general and for electric and electronics technicians (odds ratio, OR = 1.5). Again, the odds ratio was increased (OR=3.1) in the group classified as electric and electronics technicians.

Brownson (1990) conducted a case-control study which selected other cancers from a registry as controls and used the occupation as listed on the hospital record as an exposure measure. This study found absolutely no association between brain cancer an exposure to work in the communications industry. The odds ratio is slightly above 1.0 for the communications workers (OR=1.4), but is not significant. It would be hard to put any weight on this study. Three of these case-control studies have shown significant excess risks of brain cancer in people exposed to the electronics industry and, in one study, specifically to exposures to microwaves and RF radiation in that industry.

The third group of studies (Table 3) are those which specifically focus on cohorts of individuals known to be exposed to either microwaves or radio waves. In the first cohort, Lilienfeld (1978) studied individuals who were exposed to microwaves as a jamming device when stationed in the American embassy in Moscow. The study compared individuals from that embassy and those from other embassies in various parts of the world. This study collected specific questionnaire data on disease and cancer and tried to estimate the actual SAR of these individuals, which was very low. Personnel in the embassy had changed quickly. They represented both diplomatic service people as well as military personnel, making the follow-up of these individuals very difficult. Researchers took medical records for these individuals when they were part of the government service. Information on the causes of death were obtained from the records of deceased individuals. The medical records indicated a few differences such as a

Author	Subjects/Exposure	Risks
Lilienfeld 1978	4,300 employees Moscow 1,800 8,200 dependents Moscow 3,000 Questionnaire SAR est. M:2x10 <sup>-4</sup> F:7x10 <sup>-4</sup>	Medical:Increased protozoal infections.Others not clearDeaths:All cancer0.84Brain0Leukemia2.5(0.3, 9.0)Breast4.0(0.5, 14.4)
Robinette 1977, 1980 Milham 1988	40,000 veterans General division Radar operator and others Radar operators-low Gunfire control and electronics techhigh SAR $\leq 0.05$ Amateur radio	Cancerdigestive1.14respiratory1.14lymphomhemo1.19Highest exposedCirculatory dis.Cincers: resp.2.20lymphohemo1.64AML = 1.76*Sig.
	67,829 licenses (1979-84) Est. expos license expertise to determine exposure	Other lymphatic and mult. myeloma 1.62*Sig. No difference by license level
Hill 1988	Developed radar at MIT 1,492 males Est. expos old radar systems 0.1 to 0.4 W/Kg SAR Expos related job class	All cancers1.09(0.08, 1.45)lymphomas2.12(0.59, 5.42)leukemias0.64(0.08, 2.30)Hodgkins10.34(2.13, 30.23)Brain1.07(0.22, 3.13)Gall bladder/bileducts14.29(1.69, 50.29)Use of physician controls decreased Hodgkins(4.0) but gall bladder high (11.3) and found riskfor melanoma (3.8 NS)
Samigielski 1988	Polish military Expos. MW and RF	Increased incidence hemotolympho ea. 50.8/7.4 RR=6.8

Table 3. Cohort Studies With Specific Exposures

significantly increased risk of protozoal infections, which probably occurred by chance. The investigators commented that the employees of the Moscow Embassy more frequently reported the occurrence of ill-defined symptoms such as headache and fatigue but they discounted these findings.

The study demonstrated no significant excess risks associated with work at the Embassy. However, the risks of death from leukemia and breast cancer deserve comment because of observations in other studies. There was a 2.5-fold excess risk of leukemia and a 4.0-fold risk of breast cancer which were non-significant and based on small numbers. The finding on breast cancer was noted only because there has been some suspicion that, at least in very low frequency EM fields, there may be an effect on melatonin production and cycling. This population was followed shortly after initial exposure, and therefore, the latency for development of cancer was limited.

In two studies, Robinette (1977, 1980) determined the deaths of veterans who worked in areas where microwave or radar or RF exposures would have occurred. Robinette combined them into one group and initially analyzed the total population and found several non-significant excesses of 1.1 or so.

In a subsequent nested case-control study, the investigators looked at specific exposures related to the jobs of subjects. The highest exposures were in the gun control and electronics areas. For this group, there were no significant differences in the risks of any disease although the odds ratio for respiratory cancers (OR=2.2) and for lymphomas (OR=1.6), were above 1. Both of these studies do not provide evidence of any risks from RF exposures but the follow-up of the exposed individuals is short.

Milham (1988) followed a cohort of 67,829 amateur radio operators from 1979-1984. Exposure level was estimated by the type of license issued. This study reported significant increased risks of acute myelogenous leukemia (SMR=1.76) and lymphomas and multiple myeloma (SMR=1.62). There were no changes in risk according to the type of license.

Hill (1988) has reported in a thesis on a follow-up of 1,492 men who helped develop radar. The exposures were estimated to be higher than those in the other studies and were related to jobs. Despite the small size of the population, the investigator reported non-significant excesses of lymphomas and melanoma and significant and high risks of 10.3 and 14.3 for Hodgkins disease and gall bladder and bile duct cancers, respectively.

Samigielski (1988) reported on Polish military who had exposure to microwaves and RF. Very few details of the study population were provided, but the authors report an increased relative risk of 6.8 for hematolymphopoietic cancers.

In summary, the data on the possible risks associated with RF exposures differ somewhat depending on the type of study design and the focus of the study. Those studies which have examined cohorts who might have had exposure to any non-ionizing radiation have found few cancer risks except possibly leukemia, when all studies are combined, and melanoma. In some of these studies, the risks appear to be in telecommunication workers but no exposures are documented. The case-control studies emphasize brain cancer and RF exposures. The best of these studies suggests that there may be an excess risk of brain cancer in electronics workers who have RF exposures. The cohort studies of workers exposed to microwaves, radar, or radiowaves were generally negative and had short follow-up. Those studies which did report risks usually found cancers of the lymphohematopoietic system. In general, the evidence of a carcinogenic effect from RF is weak.

An examination of the literature to determine whether there is any evidence of non-cancer effects from RF reveals even less information and much of it is old (Table 4). Studies of reproductive effects report very few significant findings, and results differ from study to study. Decreased sperm counts have been reported in exposed males (Lancranjan, 1975; Buiatti, 1984). Brain tumors have been reported in the offspring of exposed males (Spitz 1985; Johnson 1989). Fetal malformations or death have also been reported (Sigler 1965; Cohen 1977; Kallen 1982). Several studies on the effect of exposures of the lens of workers in military installations show no changes. A single proportional mortality ratio (PMR) study suggested that suicide was higher in radio operators (Baris 1990). A study of neurologic effects on exposed workers showed no changes in either psychometric or neurologic tests in exposed workers although there was an abnormal increase in a single protein band in the cerebrospinal fluid. The latter finding could not be tied to any physical changes. Because of the small number of studies examining other possible effects from exposure to RF non-ionizing radiation, it is difficult to draw any conclusions.

In conclusion, studies of the effects of RF and microwave radiation are not adequate to determine whether there are any effects on humans from these exposures.

# Table 4. Other Effects

Author	Subjects/Exposure	Risks		
Reproductive Effects				
Sigler 1965 and Cohen 1977	Paternal exposure as radar operator	Downs Syndrome <u>+</u>		
Kallen 1982	2,018 Swedish physio therapists	No difference with national comparison Internal comparison: Iner. in dead and malform. infants with • short wave exposure		
Lancranjan 1975	31 exposed males 30 non-expos.	Examination spermatic fluids and hormones No hormone change Stat. sig. decrease in sperm		
Buiatti 1984	Case/control History of radio elec-work	Azoospermia/oligo spermia OR = 5.89 (0.86, 40.8) NS		
Spitz 1985	Occup. birth cert. (157 neuroblastoma) Electronics	CNS cancers in offspring and fathers occupation 11.75 (1.40, 98.5)		
Johnson 1989	Occup. birth cert. (449 CBNS cases) Electronics manufacture Radio operators	CNS cancers in offspring and fathers occupation 3.56 (1.04, 12.2) 2.01 NS		
	Ocular Eff	ects		
N/A	One study cataracts: medical records military populations or installations	Neg.		
N/A	Five studies military populations or installations Ophthalmology exam: slit lamp.	1 changes in lens 4 no changes in lens		
Neurological Effects				
Baris 1990	Mech. radar/radio TV/radio operators	Suicide mortality: PMR 153 (92, 239) 256 (123, 471)		
Nilsson 1989	17 expos. 12 non-expos.	No psychometric or neurologic changes in tests. Increase in protein band, CSF		

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# RESPONSES OF LABORATORY MAMMALS TO RADIOFREQUENCY RADIATION (500 kHz-100 GHz)\*

Joe A. Elder\*\*

## INTRODUCTION

This report is a review of selected papers describing responses of laboratory mammals exposed to radiofrequency (RF) radiation that, in keeping with the goals of this conference, 1) focuses on the frequency range from 500 kHz-100 GHz; 2) discusses important studies published since the completion of the EPA review entitled "Biological Effects of Radiofrequency Radiation" (Elder and Cahill 1984) as well as pre-1984 reports that support conclusions and generalizations regarding biological effects of RF radiation in the following subject areas—lethality, thermoregulatory responses, development, immunology, nervous system, ocular effects, life span, and cancer; 3) addresses some issues remaining unresolved since publication of the EPA review; and 4) comments on the experimental animal data used to establish the adverse effect level from which voluntary public and occupational exposure guidelines for RF radiation were developed by the National Council on Radiation Protection and Measurements (NCRP 1986) and the Institute of Electrical and Electronics Engineers (IEEE 1992); the latter guidelines were adopted by the American National Standards Institute (ANSI 1992).

## LETHALITY

A few studies describe exposure conditions that cause lethality in laboratory mammals and provide information that helps explain the cause of death from exposure to high-intensity RF radiation. Michaelson et al. (1961) conducted an experiment with a dog that showed how rectal temperature changed during an 85-min exposure at 2790 MHz (pulsed) at a dose rate (specific absorption rate, SAR) of 6.1 W/kg. Three phases of the animal's response were described. During the first phase (0-25 min), called the initial heating phase, the temperature increased about 2°C. The animal exhibited panting and an increased respiratory rate. During the second phase (25-65 min) called the thermal equilibrium period, the temperature remained at the elevated level. After 65 min of exposure, the temperature began to increase rapidly and within the next 20 min the temperature exceeded 42°C (107.6°F). Phase 3 (65-85 min) was characterized as breakdown in thermal equilibrium and collapse. In the authors' words, the temperature "continues increasing rapidly until a critical temperature of 107°F, or greater, is reached. If exposure is not stopped, death will occur" (Michaelson et al. 1961, p. 352). Other results showed that an SAR equal to about 60% of the lethal level could be tolerated for several hours, i.e., 3.7 W/kg for up to 6 h did not cause a critical rectal temperature in dogs. The work of Michaelson et al. (1961) and other investigators not cited here shows that lethality in laboratory mammals exposed to high-intensity RF radiation is caused by heat stress resulting from absorbed RF energy.

Berman et al. (1985) determined exposure conditions causing lethality in rats and displayed the data in plots of probability of lethality with time of exposure and different ambient temperature. The threshold SAR for lethality for a 4-h exposure (2450 MHz) at an ambient temperature of 30°C was about 4 W/kg. If the animals were exposed for the same duration (4 h) but at a lower ambient temperature

<sup>\*</sup> This paper has been reviewed in accordance with U.S. Environmental Protection Agency policy and has been approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use. This paper was updated in February 1995.

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(20°C), the lethality threshold increased to about 7 W/kg. These data provide support for the following general conclusion: effective SARs for thermal effects in laboratory mammals are reduced when RF exposure occurs at higher ambient temperature (Elder 1984a). A similar point is made in F.G. Shellock's paper in these proceedings that described responses of human beings exposed to RF radiation in magnetic resonance imaging (MRI) devices. At 6 W/kg, the increase in body temperature measured at the tympanic membrane was greater in a warm (33.8°C) than in a cool environment (22°C) (Shellock 1995).

The Rhesus monkey is more similar in its anatomical structure and also its thermoregulatory ability to the human being than many laboratory mammals such as the dog, rat, and mouse. For these reasons, thermoregulatory experiments have been done with Rhesus monkeys exposed to RF radiation. The results show that the rectal temperature of a Rhesus monkey exposed at 5 W/kg (225 MHz) rose to 41.5°C in about 90 min (Lotz 1985). Exposure was terminated when the temperature reached 41.5°C because the experimenters knew that possible irreversible damage (i.e., death) may occur if the exposure continued and the rectal temperature increased above 41.5°C (106.7°F). Exposure to a higher SAR greatly reduced the time to reach the critical temperature. At 10 W/kg, for example, the rectal temperature of the monkey reached 41.5°C in just a few minutes. In human beings, a core temperature of this magnitude is at the limit of tolerance at which a healthy person is likely to develop heat stroke (Athey 1992; Hardy and Bard 1974).

The papers cited here help define the dose rates and other exposure conditions that cause death and significant thermal stress in a variety of laboratory animals. With regard to frequency, the worst case scenario would be exposure of the animal to its resonant frequency, the frequency at which RF energy is maximally coupled into the animal and maximal heating occurs (D'Andrea et al. 1977). Resonant conditions occur when the wavelength of the incident RF radiation is comparable to the physical dimension of the body (Weil and Rabinowitz 1984). The resonant frequency for the adult rat is about 600 MHz. Behavioral and thermal effects in rats exposed below, at, and above resonance were reported by D'Andrea et al. (1977). The study by Lotz (1985) was designed to investigate responses in Rhesus monkeys exposed to a frequency (225 MHz) near their resonant frequency. In summary, the experimental results indicate that exposure to RF radiation at SARs ranging from 5-7 W/kg for 1.5-4.0 h at normal laboratory temperatures of 20-24°C, will cause lethality and severe thermal stress in the Rhesus monkey, rat, and dog (Elder et al. 1989).

## THERMOREGULATORY RESPONSES

RF intensities at lethal and sublethal levels can activate thermoregulatory effectors such as evaporation, vasodilation and behavior. Some of these effectors were activated in the dog in the Michaelson et al. (1961) experiment, e.g., the animal panted to increase evaporative water loss to cool its body. In heat-stressed animals including those exposed to RF radiation, cutaneous vasodilation raises skin temperature leading to increased heat dissipation. Animals may also take some form of behavioral adjustment to avoid hot environments if at liberty to do so. Animals in relatively cool environments exposed to RF radiation lower their metabolic heat production and thereby lower the overall heat load from RF energy absorption (Adair and Adams 1982, Gordon and Long 1987).

Sufficient information is available to draw a general conclusion regarding the SARs that affect metabolism and thermoregulatory effectors such as evaporation, vasodilation and behavior. The conclusion is based on a comparative analysis of the SARs that activate these four physiological responses in the mouse and squirrel monkey (Elder et al. 1989). For the smaller animal, the effective SAR to activate these responses varied from 5.3 to 29 W/kg (Ho and Edwards 1977; Gordon 1982, 1983, 1984); the effective SAR for the larger animal, the squirrel monkey, varied from 0.6 to 1.5 W/kg (Adair 1981; Adair and Adams 1980ab, 1982). These data illustrate the general principle that the larger the animal, the lower the dose rate (SAR) to activate physiological responses (Gordon 1982, Elder et al. 1989).

#### RESPONSES OF LABORATORY MAMMALS TO RF RADIATION (ELDER) 89

In related work, Gordon determined the SAR that caused a rectal temperature increase of 1°C in four different species (mouse, hamster, rat and rabbit) (Gordon et al. 1986, Gordon 1992). The results showed that the SAR to cause a 1°C rise in body temperature decreased with the mass of the animal, i.e., the mouse, the smallest animal, required the highest SAR to elevate its body temperature by 1°C. This observation is explained by the more efficient heat loss by small animals due in part to their large surface-area-to-body-mass ratio (Gordon and Ferguson 1984). It has been suggested that dose rate expressed in terms of body surface area (i.e.,  $W/m^2$ ) rather than body mass (i.e., W/kg) would allow more reliable prediction of thermal effects across species (Gordon 1987, 1992). These observations should be considered carefully when interpretating and comparing RF radiation effects in the laboratory species used in Gordon's study.

An important issue is how well Gordon's data predicts temperature responses in other species including non-human primates and human beings exposed to RF radiation. Extrapolation to animals similar in mass (4.2-6.5 kg) to the Rhesus monkeys used in studies by Krupp (1983) and Lotz (1985) indicates that an SAR of less than 1 W/kg would increase body temperature by 1°C in 1 h. The experimental results show that a higher SAR is required. In monkeys exposed near resonance, Krupp (1983, see Fig. 3) found that about 3.5 W/kg and Lotz (1985, see Fig. 2) showed that about 2.5 W/kg would cause a 1°C rise in rectal temperature in 1 h. The relationship described by Gordon between body mass and SAR causing a 1°C rise in body temperature in 1 h may apply best to small, heavily-furred laboratory animals on which the supporting data were derived.

Extrapolation of Gordon's data to a larger mass, 70 kg, the mass of the typical adult male human being, indicates that a relatively low SAR of 0.1 W/kg would raise human body temperature by 1°C in 1 h. The accuracy of this prediction cannot be determined because of the lack of human data showing a relationship between RF exposure conditions and body temperature comparable to the animal data collected by Gordon et al. (1986). The animals were exposed whole-body to a frequency at or near resonance that would cause deep-body heating whereas reports of human thermal responses to RF radiation have usually involved localized exposure of body areas. MRI studies, for example, provide SAR and human body temperature data but these results are not comparable to the data in Gordon et al. (1986) because 1) MRI exposure is generally partial-body exposure and 2) the exposure results in maximal heating at the surface of the exposed body area and minimal heating at the center of the body area (Shellock 1994). These two reasons help to explain why MRI data are in poor agreement with Gordon's prediction, i.e., MRI exposure for 20-30 min at SARs much greater than 0.1 W/kg do not elevate body temperature by 1°C. The results presented in Shellock's paper in these proceedings show that a relatively high SAR (6 W/kg) caused a 0.4°C increase in human body temperature.

The thermoregulatory ability of laboratory mammals is known to be limited in comparison to that of human beings (Adair 1983, Gordon 1993). This limitation contributes to the difficulty in extrapolation of thermal regulatory effects in furred laboratory animals, such as mice, rats, and dogs, to the human being. Regardless of the comparative abilities for thermal regulation of laboratory animals versus human beings, the absolute value of temperature increase appears to cause similar responses in these mammals at the molecular and cellular level. As temperature increases, enzymatic rates increase and metabolic pathway dynamics are altered. High temperature may cause denaturation of enzymes and other proteins resulting in irreversible molecular and cellular damage that may affect the animal adversely.

If the body core temperature approaches 42°C, an increase of about 5°C above the normal temperature of human beings and many laboratory mammals, severe thermoregulatory distress develops and death may occur if the thermal insult continues over many minutes at normal or elevated ambient temperatures. The reader is probably well aware of the concern for possible irreversible health consequences resulting from prolonged elevated body temperature in children and adults during episodes of fever. Concern for work environments that may cause a significant increase in body temperature is documented in the recommendation from the American Congress of Governmental Industrial Hygienists (ACGIH) that workers cease activity in environments that cause a 1°C rise in body temperature (ACGIH)

1990). Recognition of the potential adverse effects of increased body temperature resulting from any exposure condition or agent, including RF radiation, influenced the exposure limit recommended by the panel advising the Food and Drug Administration (FDA) on MRI devices. The panel recommendation states that "the patient is exposed to radiofrequency magnetic fields insufficient to produce a core temperature increase in excess of 1°C" (FDA 1988, p. 7577).

Thermoregulatory behavior was one of the effectors mentioned above that may be used by an animal to adjust to hot and cold environments. There are other types of behavior such as learned behavior, i.e., the performance of a learned task, that have been shown to be affected by conditions that elevate body temperature. The literature describing the effect of RF radiation on learned behavior in laboratory animals is very important because 1) the results show that dose rate (W/kg), not incident power density (mW/cm<sup>2</sup>), is the better predictor of biological effects and 2) the results have been used to define the hazardous effect level that is the basis for the voluntary RF safety guidelines published by the NCRP (1986), IEEE (1992), and ANSI (1992). No public exposure guidelines for RF radiation have been promulgated by the Federal government.

A brief description of the experimental protocol will aid an understanding of the significance of any disruption in an animal's performance of a learned task. In a typical protocol, animals are fed a restrictive diet to maintain the animal's weight below normal because a hungry animal can be trained to perform for a food reward. An animal, for example, can be trained to press a bar or button a specific number of times in a specific period of time. When the task is done correctly, the animal earns a food reward. When trained animals are exposed to noxious agents such as toxic chemicals or high-intensity RF radiation, the performance of the learned response may be detrimentally affected, i.e., the hungry animal reduces or ceases its effort to work for food. Disruption in an animal's performance of a learned task is used as a sensitive indicator of exposure to noxious chemicals and stressful environmental agents. Work disruption is a descriptive term for this effect on learned behavior.

A number of reports describe the effect of RF radiation on work disruption in several laboratory animal species (rats, squirrel monkeys, and Rhesus monkeys) exposed to different frequencies and various intensities (de Lorge 1976, 1979, 1983, 1984). Review of the data shows that the range of threshold values expressed in incident power density of RF radiation varied over a much greater range than threshold values expressed in dose rate (SAR). The threshold power densities that caused work disruption in the Rhesus monkey, for example, varied with frequency from 8 to 140 mW/cm<sup>2</sup>, a factor greater than 17. Threshold SARs, on the other hand, ranged from 3.2 to 8.4 W/kg, a factor less than three (NCRP 1986, Table 12.1). These data support the conclusion that SAR is a better predictor of biological response than power density. For this reason, the effective SAR is given for each of the biological responses discussed in this report.

As mentioned above, the data on learned behavior were used to derive the hazardous effect level in exposure guidelines developed by NCRP (1986), IEEE (1992) and ANSI (1992). The relatively narrow range of dose-rate threshold values (3.2-8.4 W/kg) for work disruption despite a considerable difference in radiofrequency (400 to 5800 MHz), species (rodents and monkeys), and exposure parameters (continuous wave and pulsed-modulation exposures, near- and far-field exposures, etc.) led to the choice of 4 W/kg for the hazardous effect level (IEEE 1992).

There has been considerable debate on whether or not the voluntary RF exposure limits developed in the United States are "thermal guidelines." In my judgement, the crux of the debate rests with the question: is the hazardous effect level based on thermal effects of RF radiation? The answer is yes. The dose-rate threshold for work disruption, the basis for the guidelines, is associated with an increase in body temperature. Since the hazardous effect level defined in the NCRP, IEEE, and ANSI guidelines is an SAR associated with an effect resulting from a known mechanism of interaction (RF heating), the guidelines are protective of effects arising from a thermal mechanism, but not from all possible mechanisms (EPA 1993).

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The association between dose-rate threshold and body temperature increase is acknowledged explicitly in the guidelines recently published by IEEE and ANSI by the statement reading "...potentially harmful biological effects were based on the disruption of ongoing behavior associated with an increase of body temperature in the presence of electromagnetic fields" (IEEE 1992, p. 27). Review of the data for the Rhesus monkey, for example, showed that the body temperature increase varied from 0.8 to 1.4°C at the SAR threshold for work disruption at four different frequencies (Elder 1994). Recently published British NRPB (National Radiological Protection Board) exposure guidelines for RF radiation are principally based on acute thermal effects. These guidelines state that "Heating is a major consequence of exposure to RF (including microwave) radiation. Restrictions on exposure are intended to prevent adverse responses to increased heat load and elevated body temperature" (NRPB 1993, p. 2). The interim nature of RF guidelines is evident because human safety limits are based principally on effects of acute exposure of laboratory animals that cause a significant increase in body temperature. Acute exposure data have been used because few studies have employed long-term, low-level exposures typical of environmental exposure to RF radiation.

#### **DEVELOPMENTAL EFFECTS**

Effective dose rates for developmental effects in laboratory animals have progressively decreased during the past decade. The 1984 EPA review states that developmental effects in laboratory animals occur at SARs greater than 15 W/kg and that these effects are definitely associated with thermal stress as indicated by increases in body temperature. The update (Elder 1987) of the conclusions in the 1984 review states that effective dose rates for developmental effects range from 9-11 W/kg based on results by Berman et al. (1982) and Lary et al. (1982,1986). These values were derived from acute exposure studies. As discussed below, a lower threshold for developmental effects was observed in rats exposed chronically to RF radiation.

Why, one might ask, should there be concern for developmental effects at 9-11 W/kg when earlier text reported death in the same species (rat) at a lower dose rate (7 W/kg)? The 7 W/kg threshold for rat lethality was based on a 240 min exposure; the developmental studies, on the other hand, usually employed a shorter exposure of 100 min. In addition to duration of exposure, effects in laboratory animals are known to be related to dose rate, radiofrequency, body mass, ambient temperature, and other factors.

In one of the few chronic exposure studies of developmental effects, Berman et al. (1992) exposed pregnant rats for 22 h/day for 19 days of the rat's gestational period of 20-21 days; ambient temperature was 22°C. Developmental effects were observed at 4.8 W/kg, a value about half of the threshold observed in acute exposure studies summarized above; the lower effective dose rate was attributed to chronic exposure. Lower SARs (0.07 and 2.4 W/kg) did not cause developmental effects in chronically exposed rats. In the published paper, Berman et al. attributed the effect at 4.8 W/kg to thermal stress that caused the death of two of 12 animals in the highest exposure group. In summary, the developmental studies show that RF radiation is a teratogen, but effective dose rates during acute and chronic exposure approach lethal levels for pregnant animals due to thermal stress.

The above conclusion is based on a synthesis of results from a significant number of reports that together demonstrate that developmental effects are associated with a significant body temperature increase. This set of literature does not include a paper reporting developmental effects in rats at 0.0001 W/kg, an SAR thousands of times less than the effective SARs cited above. This very low SAR would not cause a significant body temperature increase in the rat and is characterized as a nonthermal exposure. Further work is needed to confirm or refute the finding of developmental effects in rats exposed to nonthermal levels of RF radiation as reported by Tofani et al. (1986).

#### IMMUNOLOGY

The Chou et al. (1992) study, commonly known as the University of Washington study, was a chronic exposure study in which rats were exposed to 0.15-0.40 W/kg for 21.5 h/day for up to 25 months. These relatively low dose rates and an ambient temperature of 21°C would have combined to minimize any significant effect on body temperature which was not measured. Based on other measures of thermoregulation (oxygen consumption, carbon dioxide production, food consumption, etc.), the authors concluded that the rate of RF energy deposition was not sufficient to produce robust changes in the metabolism of mature rats. The study evaluated 155 biological parameters including immune responses.

After 13 months of exposure, a significant effect on the immune system was found but the effect was not observed after 25 months of exposure. In a follow-up study done by these researchers, the stimulatory effect observed in the original study was not confirmed (Chou et al. 1992). The absence of a reproducible immune response in the two University of Washington studies is consistent with the following conclusions in a review of in vivo immune effects: 1) many if not all of the RF-induced alterations in the immune system can be attributed to a nonspecific thermal stress response, and 2) studies investigating the reversibility of immune responses have shown the effects to be transient (Smialowicz 1987). Future research should address the physiological significance, if any, of transient immune responses in laboratory animals exposed to RF radiation.

## **NERVOUS SYSTEM**

The nervous system is considered to be one of the more sensitive systems to RF radiation. Recent studies on the effects of low dose rates on the efficacy of nervous system drugs and on the blood-brain barrier have been selected to describe the sensitivity of the nervous system to RF radiation.

Work in Lai's laboratory showed that the efficacy of some nervous system drugs was affected by dose rates as low as 0.1 to 0.6 W/kg; some effects of drugs were enhanced while other effects were attenuated (Lai 1992). Based on the similarity of the effects of RF radiation and those of established sources of stress, Lai (1992) speculated that RF radiation is a stressor. Reports showing that RF radiation affects neural mechanisms known to be involved in stress responses provide additional support for this hypothesis (see Lai 1992). Another important conclusion was the lack of convincing evidence that repeated, acute RF radiation exposure (45 min at 0.1-0.6 W/kg) caused irreversible neurological effects (Lai 1992).

There were reports in the 1970's describing effects of RF radiation on the blood-brain barrier, the unique physiological system in the brain that prevents entry of unwanted molecules. These studies were especially interesting because the results indicated an important effect on the central nervous system at nonthermalizing levels of RF radiation. A number of studies in the 1980's, however, failed to confirm and extend the earlier results on the blood-brain barrier. While there is the criticism that no effects were observed at low exposure levels because the studies were not true replicates of the earlier experiments, these and other studies did validate that thermal insults caused at high SARs will disrupt the integrity of the blood-brain barrier (Ward et al. 1982, Lin and Lin 1982, Williams et al. 1984, Ward and Ali 1985).

A recent paper by Salford et al. (1993) has refocused attention on the blood-brain barrier as a system that should be investigated further. These investigators reported effects on the blood-brain barrier in mice exposed at 900 MHz at a low SAR (0.33 W/kg). An independent validation of this result is needed and, if successful, effective exposure conditions and threshold SAR need to be determined.

## **OCULAR EFFECTS**

It is well documented that acute exposure to the rabbit eye can cause cataracts, but the effective SAR that causes cataracts is very high (150 W/kg). The animal survived the cataractogenic exposure

because the exposure to the eye that developed a cataract was so localized that the other eye served as the control. A substantial temperature increase in the lens of the eye is associated with cataract formation, thus demonstrating that cataracts are caused by a thermal mechanism, i.e., the proteins in the lens are denatured by heat resulting from the absorbed RF energy (Elder 1984b).

In recent studies with monkeys concerning ocular effects other than cataracts, effects on cells in the cornea and effects on permeability in the iris were observed at 2.6 W/kg. Pretreatment of the eye with an ocular drug (timolol) reduced the effective dose rate by a factor of 10 to 0.26 W/kg (Kues et al. 1992). In a preliminary report, D'Andrea et al. (1993) reported no effect on visual performance in monkeys exposed to RF radiation conditions similar to those reported by Kues et al. to cause ocular effects. At this time, the level of concern for the low SAR-induced ocular effects reported by Kues et al. (1985, 1992) is attenuated by lack of independent replication of these results.

#### LIFE-SPAN AND CANCER

There is convincing data in the chemical toxicity literature that show a positive correlation between decreased life-span and increased cancer development, especially for leukemia and mammary tumors. The data were reported by Haseman and Rao (1992) who compiled and analyzed data from 88 two-year cancer bioassay studies sponsored by the National Toxicology Program. Both human leukemia, animal mammary tumors, and other cancers are mentioned in the RF literature (Milham 1988, Szmigielski et al. 1982). The latter paper reported that survival time of mice exposed to RF radiation was significantly shorter due to the earlier appearance of mammary tumors and benzopyrene-induced skin cancer. The discussion here addresses the strength of the association between decreased life-span and increased cancer development in RF-exposed animals (Elder 1994).

Seven animal studies reporting data on life-span utilized a variety of experimental conditions including different species, frequencies, modulation, and dose rate (Prausnitz and Susskind 1962, Spalding et al. 1971, Preskorn et al. 1978, Szmigielski et al. 1982, Santini et al. 1988, Chou et al. 1992, Liddle et al. 1994). Six of the seven studies used mice; rats were used in the University of Washington study (Chou et al. 1992). It is interesting that two of these studies reported a significant increase in life-span in the RF-exposed animals (Prausnitz and Susskind 1962; Preskorn et al. 1978) and two papers (Spalding et al. 1971; Chou et al. 1992) reported that the average life-span was increased but the increase was not statistically significant. The results of these four studies support a finding of no adverse effect on life-span because the data indicate a trend toward an increase in life-span of laboratory animals exposed to RF radiation rather than a decrease in life-span. No effect on survival was observed by Santini et al. (1988) who exposed mice to both continuous wave and pulsed microwave fields. Details of the exposure conditions of the studies mentioned here are given below in the discussion of the cancer results.

Two studies reported RF exposure conditions that decreased life-span. In a chronic exposure study, Liddle et al. (1994) showed no life-span effect in mice exposed 1 h/day, 5 days/wk for life, at 2 W/kg, a dose rate that would cause minimal or no thermal stress in this experiment; however, there was a decrease in life-span at 6.8 W/kg that was attributed to thermal stress. In earlier work, Liddle et al. (1987) reported that exposure of mice at 6.8 W/kg caused a maximal body temperature increase of 0.8°C within 30 min after initiation of exposure.

Szmigielski et al. (1982) exposed female mice with a high incidence of spontaneous mammary cancer to 2450 MHz for 2 h/day from the sixth week of life up to age 12 months. RF exposure at 2-3 and 6-8 W/kg reduced survival time. These authors also reported reduced survival time due to the earlier appearance of cancer in RF-exposed mice that developed benzopyrene-induced skin cancer. The animals were exposed simultaneously to benzopyrene (every second day for 5 months) and RF radiation (2 h/day for 5 months). The mean survival time of 50% of the mice was 331 days for controls and 165 days at 6-8 W/kg (see Szmigielski et al. 1982, Figure 10). No detectable increase in rectal temperature was reported in mice exposed at 6-8 W/kg but there is no description of how or when temperature was

measured. The maximal temperature increase due to RF exposure may not have been observed because Liddle et al. (1987) has presented data demonstrating that timing of the temperature measurement is critical. As mentioned above, Liddle et al. (1987) reported that mice exposed to 2450 MHz at 6.8 W/kg had a maximal body temperature increase of 0.8°C. Based on these data, mice exposed at the SAR range (6-8 W/kg) in the Szmigielski et al. study did receive a significant thermal load from absorbed RF energy. In summary, the results of these seven studies indicate that life-span is not adversely affected by RF radiation unless exposure causes a significant increase in body temperature.

Five of the RF radiation studies on life-span have cancer data and three of these studies reported no increase in cancer incidence. The results of Preskorn et al. (1978) showed a delay in tumor development, but no change in total number of tumors in the RF-exposed groups. Prausnitz and Susskind (1962) concluded that the incidence of cancer of the white cells was not significant. In both studies, mice were exposed to very high SARs [40 W/kg, 4.5 min/day, 5 days/wk, 59 wks in Prausnitz and Susskind's study and 35 W/kg, 20 min/day, 4 days (prenatal) in Preskorn et al.'s study]. Microwaves did not affect tumor development in mice exposed 2.5 h/day, 6 days/wk to either continuous wave or pulsed fields at 1.2 W/kg (Santini et al. 1988). In this experiment, female mice at age 35 days were exposed to microwaves 15 days prior to implantation of melanoma cells until death (up to 690 h of irradiation).

Two chronic exposure studies reported statistically significant effects. Chou et al. (1992) exposed rats at 0.15-0.40 W/kg for 21.5 h/day for up to 25 months and found a statistically significant increase in malignancies when all types of malignancies were summed. In their interpretation of the biological significance of the increase in malignancies, the authors were influenced by their data on life-span. Rather than a decrease in life-span, they found an increase although the increase was not statistically significant. The authors concluded therefore that the biological significance of the cancer incidence is questionable. There has been much discussion about the validity of the summing procedure resulting in the statistically significant increase in cancer. Most importantly, further work is needed to confirm or refute the finding of increased cancer incidence in rats exposed chronically to low dose rates as reported by Chou et al. (1992). The life-span data, the controversial summing procedure, and the lack of replication support the conclusion that the Chou et al. (1992) study does not prove a cause-and-effect relation between RF radiation and cancer.

In experiments involving exposure durations of several months, Szmigielski et al. (1982) observed that SARs of 2-3 and 6-8 W/kg increased cancer incidence in three different models: spontaneous mammary tumors, benzopyrene-induced skin cancer, and lung tumors. These researchers also found that mice subjected to chronic confinement stress and mice exposed at 2-3 W/kg had a similar increase in tumor development; these results were significantly different from control values. Szmigielski et al. discussed speculations to explain their findings of increased cancer incidence from chronic confinement stress and RF radiation. While the results are suggestive of an association between RF radiation and cancer development in mice, the scientific process required to prove a cause-and-effect relationship is not complete. In the 13 years since publication of the Szmigielski et al. paper, no independent replication of the experiments has been reported in the literature. Information on the replicability of these findings is an important void in our knowledge of the carcinogenic potential of RF radiation.

In my opinion, the conclusion that no causal relationship has been established between cancer and RF radiation seems consistent with the life-span data showing no detrimental effect in the absence of thermal stress from RF exposure. The author notes that this conclusion is based on a few studies that used very different exposure conditions and biological models to collect data on life-span and cancer in laboratory mammals. In the author's opinion, the data on cancer and life-span effects in laboratory mammals are not useful in revision of voluntary RF exposure guidelines developed in the U.S. because 1) there are relatively few reports that describe effects due to long-term, low-level exposure, 2) effects that have been reported have not been independently replicated, and 3) dose-rate/response relationships have not been established.

## SUMMARY

The literature describing responses of laboratory mammals exposed to RF radiation is sufficiently developed to draw the following conclusions.

- 1) Lethality in laboratory animals exposed to high-intensity RF radiation appears to be due to thermal stress, i.e., absorbed RF energy results in an increase in body temperature beyond life-sustaining limits.
- 2) Dose rates ranging from 5-7 W/kg for 1.5-4.0 h at normal laboratory temperatures of 20-24°C will cause lethality and severe thermal stress in the Rhesus monkey, rat, and dog.
- 3) A variety of effects occur in mammals exposed at sublethal RF intensities associated with significantly increased body temperature. Such exposure can cause birth defects and affect the thermoregulatory system, immune system, blood-brain barrier and behavior. Developmental effects, for example, result from acute and chrohic RF exposures that approach lethal levels for pregnant animals due to thermal stress. Cataracts have been caused in some laboratory animal species by sublethal, localized exposure that significantly increased the temperature in the lens of the eye.
- 4) Although there are major thermoregulatory differences between laboratory animals and human beings, the absolute magnitude of body temperature increase appears to correlate well with many similar molecular, cellular, and physiological effects in these mammalian species.
- 5) Dose rate (specific absorption rate, SAR, expressed in units of W/kg) is a better predictor of biological response than power density (e.g., mW/cm<sup>2</sup>).
- 6) Effective SARs for thermal effects are reduced when RF exposure occurs at higher ambient temperatures. Humidity, air flow, and other ambient factors that affect thermoregulation would also influence effective SARs for biological responses in mammals.
- 7) Effective SARs for thermal effects in small laboratory animals are higher than for larger animals because, in part, of more efficient heat loss by small animals due to their larger surface-to-mass ratio.
- 8) In the absence of thermal stress, no adverse effect on life-span of RF-exposed laboratory animals has been substantiated.
- 9) No effect on life-span in the absence of thermal stress is consistent with the conclusion that no causal relationship has been proven between RF radiation and cancer incidence in laboratory mammals. The author notes that the conclusions on life-span and cancer are based on a small number of studies that used very different exposure conditions and biological models.

The data on cancer and life-span effects in laboratory mammals, in the author's opinion, are not useful in revision of voluntary RF exposure guidelines developed in the U.S. because 1) there are relatively few reports that describe effects due to long-term, low-level exposure, 2) effects that have been reported have not been independently replicated, and 3) dose-rate/response relationships have not been established.

Specific biological effects described in this paper that have been reported to occur in laboratory mammals exposed to low dose rates of RF radiation include the following: 1) the statistical significant cancer incidence in rats exposed at 0.14-0.4 W/kg in the University of Washington study (Chou et al. 1992); 2) effects on the primate eye at 0.26 W/kg (Kues et al. 1985,1992); 3) blood-brain barrier changes

at 0.33 W/kg (Salford et al. 1993); 4) drug potentiation effects in the central nervous system at 0.1-0.6 W/kg (Lai 1992); and 5) developmental effects in rats exposed to 0.0001 W/kg (Tofani et al. 1986). These effects can be characterized as having been reported in a singular paper or in a series of papers from one research team. The independent replicability of these observations, therefore, is very important to an assessment of the potential health effects of RF radiation. Further research is needed to confirm or refute potentially significant biological effects, including cancer, blood-brain barrier and other central nervous system alterations, developmental effects, and ocular effects, that have been reported in laboratory mammals exposed at low levels of RF radiation. Also, comparative studies of thermoregulatory responses in mammals exposed to RF radiation would aid extrapolation of data across species, including human beings.

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# **RADIOFREQUENCY RADIATION EFFECTS ON CELLS\***

Stephen F. Cleary\*\*

## INTRODUCTION

Mammalian cells or biomolecules exposed <u>in vitro</u> afford a unique opportunity to investigate biological effects of radiofrequency electromagnetic radiation (RFER) under conditions of precise experimental control of variables including: (a) induced electric (E) or magnetic (B) field strength; (b) modulation; (c) dose rate or specific absorption rate (SAR); (d) temperature; and (e) composition of cell exposure medium. The interaction of RFER with mammalian cells and biomolecules is also amenable to theoretical determination of the magnitude and spatial distribution of induced E and B fields and hence cell or molecular level SAR distributions. Consequently, mammalian cells and biomolecules provide the most direct approach to determining basic interaction mechanisms of RFER biological effects. <u>In vivo</u> systems do not afford this opportunity due to inherent dosimetric and densitometric complexities that place practical limitations on the accuracy of E-, B-field or SAR determinations in tissue.

<u>In vitro</u> studies of the effects of RFER on various cell physiological endpoints include: (a) membrane cation transport and binding; (b) neuroelectrical activity; (c) proliferation; and (d) transformation. The results of these studies have been the subject of review articles (1-4). The primary purpose of this communication will be to review recent <u>in vitro</u> studies that: (a) provide additional insight regarding possible RFER cellular interaction mechanisms; (b) provide evidence of direct or athermal RFER cellular effects; and (c) are of potential relevance to human health effects such as reported associations of RFER exposure and cancer incidence. It is not the purpose of this communication to provide a comprehensive review of <u>in vitro</u> cellular effects of RFER (for more comprehensive reviews refer to references 1-4).

Based upon the results of the studies reviewed here it may be concluded that under some exposure conditions RFER directly alters mammalian cell physiology in the absence of indirect thermal effects. Although specific interaction mechanisms are uncertain the data suggest that the most likely interaction site for many of the cellular effects of RFER is the cell plasma membrane. Further insight regarding in <u>vivo</u> effects of RFER, such as cancer induction or promotion can be provided by appropriately designed in vitro cell studies.

## MEMBRANE CATION PERMEABILITY AND CALCIUM BINDING

Studies of cell membrane cation permeability provided the first indication of direct nonthermal effects of RFER. Exposure of human, rabbit, and canine erythrocytes to 2.45-, 3.0 and 3.95 GHz continuous wave (CW) microwave radiation at SARs of up to 200 W/kg resulted in intracellular K<sup>+</sup> leakage and osmotic lysis. Temperature control studies conducted over the same temperature range (26 to 44°C) suggested, however, that the effects were due to RFER-induced heating (5). In a subsequent study of passive cation (Na<sup>+</sup>, Rb<sup>+</sup>) efflux from rabbit erythrocytes exposed to 2.45 GHz RFER at SARs of 100,-190- and 390 W/kg statistically significant increases were detected, but only at a temperature of 22.5°C (6). In agreement with the results of Liu et al. (5), RFER had no direct effect at temperatures greater than 22.5°C. Additional evidence of direct RFER-induced membrane permeability changes in the range of 17.7 to 19.5°C was reported (7,8,9). The effect of RFER (2.45 GHz) was enhanced when

<sup>\*</sup> This paper was updated in March 1994.

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erythrocytes were exposed under hypoxic conditions or when exposed in the presence of plasma (8). Increasing the cell membrane cholesterol content or treatment with antioxidants, on the other hand, inhibited the effect of RFER exposure (8).

An indication that RFER-induced changes in cell membrane cation permeability were not highly frequency specific was provided by the results of a study of the effect of 8.42 GHz RFER on K<sup>+</sup> release from rabbit erythrocytes. Cleary et al. (10) exposed erythrocytes to SARs of 21 to 90 W/kg. Compared to temperature controls, RFER had no effect on K<sup>+</sup> release, except under conditions when the steady state temperature was maintained at 24.6°C during exposure. RFER exposure at lower or higher temperatures was ineffective. The results of these experiments (5-10) suggested an interaction between RFER exposure, cation transport, and a gel-to-liquid crystal membrane phase transition (10). Since temperature-specific effects on erythrocyte cation transport could not be induced in the absence of RFER exposure they were interpreted as a direct effect on the red cell membrane (3).

A molecular interaction mechanism for the effect of RFER on membrane cation transport was suggested by Allis and Sinha-Robinson (11). Human erythrocyte membranes were exposed to 6W/kg 2.45 GHz RFER at 1°C temperature increments between 23° and 27°C. When membrane Na<sup>+</sup>/K<sup>+</sup> ATPase activitity was monitored spectrophotometrically, it was found that enzyme activity was inhibited only at 25°C (11). This led to the hypothesis that inhibition resulted from a direct interaction of RFER with the ATPase enzyme. This interaction mechanism is consistent with reported effects of RFER on erythrocyte cation (K<sup>+</sup>, Na<sup>+</sup>, Rb<sup>+</sup>) transport at the membrane phase transition (5-10).

Evidence of direct RFER effects on cells was also revealed by a series of studies of effects on calcium  $(Ca^{+2})$  binding to nerve cell membranes. In contrast to effects on membrane cation transport, which occurred following CW or pulse modulated RFER exposure, effects on  $Ca^{+2}$  binding were strongly dependent upon RFER modulation at extremely low frequencies (ELF), most prominently 15- or 16Hz (12). The  $Ca^{+2}$  efflux response went through a series of maxima as the modulation rate or RFER intensity was increased. (13,14). These responses, referred to as frequency or power "windows" occurred under conditions not associated with RFER-induced heating. The generality of the effect was indicated by similar responses of synaptosomes (15) and neuroblastoma cells (16).

#### MOLECULAR/BIOCHEMICAL EFFECTS

Detailed mechanisms explaining molecular level biochemical effects of RFER are not yet available. Insight is provided, however, by studies of specific biomolecular interactions conducted under conditions involving different molecular microenvironments. Fisher et al. (9) detected a 40% reduction in ouabain sensitive Na<sup>+</sup> efflux from erythrocytes exposed at 23-24°C to 2.45 GHz RFER at a SAR of 3W/kg. This response was attributed to a field-induced effect on membrane Na<sup>+</sup>/K<sup>+</sup> ATPase. Using this same frequency of RFER, Allis and Sinha-Robinson (11) induced a 35% decrease in Na<sup>+</sup>/K<sup>+</sup> ATPase activity in erythrocyte membrane fragments at a SAR of 6 W/kg. Brown and Chattopadhyay (17), on the other hand, reported a 23% decrease in Na<sup>+</sup>/K<sup>+</sup> ATPase activity at 24.9°C when the enzyme was exposed in solution to 9.14 GHz CW RFER at a SAR of 20W/kg. In view of previous evidence that the effect of RFER on Na<sup>+</sup>/K<sup>+</sup> membrane transport was not highly frequency dependent (10), the results of these studies suggest that the RFER intensity needed to alter enzyme activity may depend upon the microenvironment of the Na<sup>+</sup>/K<sup>+</sup> ATPase. The fact that the minimum RFER intensity required to affect Na<sup>+</sup>/K<sup>+</sup> ATPase activity occurred in intact membranes suggests an interaction between RFER energy and metabolic energy. Maximum RFER intensity was required for Na<sup>+</sup>/K<sup>+</sup> ATPase inactivation in solution in the absence of cell metabolic energy sources. This hypothesis is supported by the results of previous studies of the effects of low-intensity RFER on biomolecules in solution which have, in general, yielded negative results (18).

Additional evidence of direct biochemical interactions of RFER was reported by Phelan et al. (19) who investigated effects on the structure of cell or liposome membranes. RFER (2.45 GHz) exposure at intensities as low as 0.2 W/kg caused a shift from a fluid to gel state in membranes that contained

melanin. In the absence of melanin, RFER exposure had no effect on membrane structure. The fact that the RFER effect was inhibited in the presence of superoxide dismutase (SOD), indicated the involvement of free radical generation (19). The results and conditions for the molecular/biochemical studies of RFER reviewed here are summarized in Table 1.

#### **MEMBRANE ION CHANNELS**

Evidence of direct athermal interactions of RFER with biomolecules other than enzymes is provided by studies of effects on membrane ion channels and excitable membranes. Sandblom and Theander (20) investigated effects of 10 GHz pulsed RFER on the kinetics of gramicidin-A-channels in artificial lipid bilayer membranes. A 1 min. exposure to short (1 µsec) high instantaneous power (350 W/kg), RFER pulses had no effect on the lifetime or conductance of gramicidin-A-channels. However, RFER exposure decreased significantly the rate of channel formation (20). Since it is well known that the rate of single channel formation increases with increasing temperature, the RFER effect was concluded to be a direct effect on the gramacidin-A-channel molecular complex. The effect was attributed to either field-induced dipole reorientation, changes in lipid conformation, or altered structure of water inside channel peptide helices (20).

A similar effect on ion channels was reported by D'Inzeo et al. (21) who briefly (30-120 s) exposed chick myotubes to CW 9.75 GHz RFER at low intensities (~1-2  $\mu$ W/cm<sup>2</sup>). RFER exposure decreased the frequency of single-channel openings of acetylcholine-induced channels. (21).

Direct effects of RFER on excitable membranes have also been reported. The rate of rapid, burstlike changes in the firing rate of molluscan neurons was increased by exposure to pulse modulated (PM) 900 MHz RFER at SARs of 0.5 W/kg or higher (22). In this range of SARs, CW RFER did not affect the neuronal firing rates. The specificity of the effect on the neuronal membrane firing rate was demonstrated by the finding that mediator-induced activation of acetylcholine, dopamine, serotonin, or gamma-aminobutyric acid membrane receptors was not affected by either PM or CW RFER (22). These studies are summarized in Table 2.

## FUNCTIONAL AND GENOMIC ALTERATIONS

A variety of <u>in vitro</u> functional and genomic cellular alterations have been attributed to direct effects of RFER exposure. Cleary et.al (23,24,25) reported altered proliferation of normal resting human peripheral lymphocytes and human or rat glioma following a 2h exposure to 27- or 2450 MHz CW or PM RFER at SARs in the range of 0.5 to 200 W/kg. Altered cell proliferation persisted for up to 5 days after RFER exposure. The effect was biphasic; maximum increased proliferation occurred at 25 W/kg whereas exposure at 50 W/kg or higher generally suppressed proliferation (25). Since cells were exposed under isothermal conditions  $(37\pm0.2^{\circ}C)$  altered proliferation was attributed occurred at 25 W/kg whereas exposure at 50 W/kg or higher generally suppressed proliferation (25). Since cells were exposed under isothermal conditions  $(37\pm0.2^{\circ}C)$  altered proliferation was attributed occurred at 25 W/kg whereas exposure at 50 W/kg or higher generally suppressed proliferation (25). Since cells were exposed under isothermal conditions  $(37\pm0.2^{\circ}C)$  altered proliferation was attributed to a direct effect of RFER. Similar direct effects of pulsed RFER on lymphoblastoid transformation were reported following a 5 day exposure to 2.45 GHz RFER at a maximum SAR of 12.3 W/kg(26).

Neoplastic cell transformation has also been reported as a direct effect of low intensity RFER exposure. Mammalian embryonic fibroblasts were exposed for 24h to 0.1, 1, or 4.4 W/kg 2.45 GHz RFER pulse modulated at 120 Hz(27). In the absence of the tumor promoter 12-0-tetradecanoyl-phorbol-13-acetate (TPA) RFER did not affect cell survival or the rate of neoplastic transformation. Cells treated with TPA and RFER experienced a statistically significant dose-dependent increase in neoplastic transformation rate. Exposure to 4.4 W/kg RFER with TPA had a neoplastic transformation effect equivalent to exposure to 1.5 Gy of X-radiation. It was determined that RFER and X-rays acted independently in inducing neoplastic transformation (27). Evidence of direct genomic effects of RFER on human somatic cells have also been reported including chromosmal aberrations (acentric fragments and
	-		
SOURCE DESCRIPTORS	TYPICAL EFFECT	FIELD PARAMETERS/ THRESHOLDS	COMMENTS
• 9.14 GHz CW microwaves	• altered Na <sup>+</sup> /K <sup>+</sup> ATPase enzyme activity	• 20 W/kg	<ul> <li>enzyme activity <u>increased</u> at temp. between 7 and 43.8°C; 23% <u>decrease</u> at 24.9°C; inhibitory effect of ouabain significantly reduced by microwave exposures at T&gt;24.9°C</li> <li>attributed to direct molecular level interaction of microwaves (Ref.17)</li> </ul>
• 2.45 GHz CW microwaves	• altered Na <sup>+</sup> /K <sup>+</sup> ATPase activity in erythrocyte membrane fragments	• 6 W/kg	<ul> <li>enzyme activity <u>decreased</u> 35% at 25°C only, not at other temp. in range 23-27°C</li> <li>ouabain-insensitive Ca<sup>+2</sup> ATPase activity also altered (Ref.11)</li> </ul>
• 2.45 GHz pulsed microwaves	<ul> <li>altered Na<sup>+</sup>/K<sup>+</sup> ATPase activity in erythrocytes</li> </ul>	• 3 W/kg	• 40% <u>decrease</u> in ouabain sensitive Na <sup>+</sup> efflux at 23 and 24°C (Ref.9)
• 2.45 GHz pulsed microwaves	• altered membrane structure in melanoma cells or melanin containing liposomes	• 0.2 W/kg	<ul> <li>microwaves induced shift from fluid to gel state in membrane in presence of melanin</li> <li>effect inhibited by SOD</li> <li>microwave effect may be mediated by temp. dependent generation of O<sub>2</sub> radicals (Ref.19)</li> </ul>

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## Table 1. MOLECULAR/BIOCHEMICAL EFFECTS OF RFER

SOURCE DESCRIPTORS	TYPICAL EFFECT	FIELD PARAMETERS/ THRESHOLDS	COMMENTS	
• 10 GHz pulsed microwaves	• single channel kinetics of gramicidin-A-channels in lipid bilayers	<ul> <li>1 μs pulse 350 W/kg instantaneous</li> <li>10<sup>5</sup> V/m instantaneous</li> <li>10<sup>3</sup> p.p.s</li> <li>1 min exposure</li> </ul>	<ul> <li>no effect on channel conductance or lifetime</li> <li>significant decrease in rate of channel formation</li> <li>opposite from heating effect</li> <li>due to direct interaction with channel-forming molecules (Ref.20)</li> </ul>	
• 9.75 GHz CW microwaves	<ul> <li>single channel kinetics of acetlycholine-induced channels in chick myotubes</li> </ul>	<ul> <li>~1-2 μW/cm<sup>2</sup></li> <li>30-120s</li> </ul>	• decreased frequency of single- channel openings (Ref.21)	
• 900 MHz pulsed microwaves	• firing rate of molluscan neurons	<ul> <li>0.5 W/kg threshold</li> <li>0.5-110pps</li> <li>2 min exposure</li> </ul>	<ul> <li>increased rates of rapid, burst-like firing</li> <li>lesser effect of CW microwaves at same SARs</li> <li>direct effect on neuronal membrane (Ref.22)</li> </ul>	

## Table 2. MEMBRANE ION CHANNEL EFFECTS OF RFER

#### 106 SUMMARY AND RESULTS OF THE RADIOFREQUENCY RADIATION CONFERENCE: VOLUME 2

dicentric chromosomes) micronuclei formation and mutagenic characteristics typical of chemical mutagens (28,29). Studies of the functional and genomic effects of RFER are summarized in Table 3.

### SUMMARY AND CONCLUSIONS

In vitro cellular and molecular level studies provide evidence of direct athermal effects of RFER on cellular processes including: (1) membrane ion transport and binding; (2) membrane structure; (3) membrane single ion channel kinetics; (4) neuronal activity; (5) proliferation/activation; and (6) neoplastic transformation. Cellular alterations were reported under a variety of exposure conditions: (1) SARs from 0.2 to greater than 100 W/kg; (2) frequencies of from 2 GHz to 50 GHz; (3) CW and PM RFER exposure. The majority of <u>in vitro</u> RFER <u>in vitro</u> studies involved acute exposures (periods of a few hours or less). There is insufficient data to define time or intensity thresholds or RFER frequency-dependence for the majority of the reported <u>in vitro</u> effects.

In spite of the limitations of the available data some general conclusions may be arrived at: (1) RFER can directly induce cell physiological alterations <u>in vitro</u> under conditions that do not involve temperature elevations; (2) although detailed mechanisms are unknown, the cell plasma membrane is the most likely RFER interaction site; (3) RFER affects a variety of biomolecular systems with no clear indication of specific molecular sensitivities; and (4) effects of RFER on mammalian cells <u>in vitro</u> are generally consistent with reported <u>in vivo</u> exposure effects including increased cancer incidence as related to effects on promotion and/or the rate of neoplastic transformation. There is an obvious need for additional data to more adequately relate <u>in vitro</u> and <u>in vivo</u> effects of RFER exposure.

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SOURCE DESCRIPTORS	TYPICAL EFFECT	FIELD PARAMETERS/ THRESHOLDS	COMMENTS
<ul> <li>27 MHz CW or pulsed</li> <li>2.45 GHz CW or pulsed</li> </ul>	• altered proliferation of human or rat glioma and human lymphocytes	<ul> <li>0.5 to 200 W/kg</li> <li>2 h isothermal (37°C) exposure</li> </ul>	<ul> <li>proliferation altered for 1-5 d postexposure</li> <li>evidence of cumulative effect</li> <li>similar effects of CW or pulsed fields</li> <li>biphasic dose rate effect (Ref. 23,24,25)</li> </ul>
• 2.45 GHz pulsed microwaves	<ul> <li>transformation of C3H/10T <sup>1</sup>/<sub>2</sub> mouse embryo fibroblasts</li> </ul>	<ul> <li>4.4 W/kg</li> <li>37.2 ± 0.1°C</li> <li>24 h exposure</li> </ul>	<ul> <li>latent transformation revealed by TPA treatment of cells exposed to X-radiation and microwaves (Ref.27)</li> </ul>
• 7.7 GHz CW microwaves	<ul> <li>chromosomal aberrations</li> <li>micronuclei formation in human lymphocytes</li> </ul>	• 0.5-,10-, 30 mW/cm <sup>2</sup> • 10-,30-,60 min	<ul> <li>higher frequency of chromosomal aberrations in all exposed samples</li> <li>increased frequency of micronuclei in exposed samples correlated with specific chromosomal aberrations (Ref.28)</li> </ul>
• 2.45 GHz CW or pulsed microwaves	• lymphoblastoid transformation of human lymphocytes	<ul> <li>5 d exposure</li> <li>1 µs pulse</li> <li>100-10<sup>3</sup> PPS</li> <li>max SAR</li> <li>12.3 W/kg</li> </ul>	<ul> <li>temperature dependent increase in control and CW microwave exposed samples</li> <li>pulsed microwaves increased lymphoblastoid transformation without heating (Ref.26)</li> </ul>

## Table 3. FUNCTIONAL AND GENOMIC EFFECTS OF RFER

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# ALTERATIONS IN ORNITHINE DECARBOXYLASE ACTIVITY: A CELLULAR RESPONSE TO LOW-ENERGY ELECTROMAGNETIC FIELD EXPOSURE\*

Craig V. Byus\*\*

#### INTRODUCTION

The enzyme ornithine decarboxylase (ODC) is, under most situations, the controlling enzyme in polyamine biosynthetic pathway (1,2). This enzyme decarboxylates, or removes, the carboxyl group from ornithine to yield putrescine or diaminobutane. Through another series of enzymatic reactions, propylamine moieties can be added sequentially to putrescine to yield spermidine and spermine, respectively. The polyamines are found ubiquitously in nature and have been most closely linked to the processes of cellular proliferation, hypertrophy and differentiation in eukaryotic cells (1,2). Use of selective inhibitors of polyamine biosynthesis and preparation of mutants lacking polyamines have presented convincing evidence that the polyamines are essential for many functions inside the cell involving macromolecules with negative charges. The polyamines possess the highest positive charge to mass ratio of any biosynthesized molecule and, in general, are believed to be highly bound inside of cells to a number of macromolecules with negative charges.

Given the enormous importance of polyamine biosynthesis for the continued proliferation and differentiation of mammalian cells, study of the regulation of this enzyme has received a considerable amount of attention. In general, in quiescent or non-growing cells, the level of ODC activity is extremely low. However, following stimulation of the cell to grow or divide by any of a number of hormones or growth factors, ODC activity can increase markedly (i.e., up to 500-fold) and rapidly from these low basal values (3). Increases in ODC have been shown to involve a number of specific molecular mechanisms including: increases in ODC-specific mRNA brought about by increases in the transcription of the ODC gene, increases in the half-life of ODC mRNA, altered translation of ODC mRNA, and increases in the half-life of the ODC protein posttranslationally (3). While all of these mechanisms have been shown to be important in specific instances, it is currently believed that to a great extent ODC activity is controlled by posttranslational mechanisms involving degradation of the enzyme in response to increases in polyamine levels (4).

Due to the high sensitivity of this enzyme to a large variety of stimuli and the involvement of changes in ODC activity and polyamines in a variety of pathologies including cancer, ODC appeared to be a logical choice to investigate as a potential marker of exposure of cells or tissues to low-energy electromagnetic fields. For these reasons we began a series of investigations to study whether ornithine decarboxylase activity was altered following exposure of a variety of animal and human cells in culture following exposure to three low-energy electromagnetic fields including low-frequency amplitude modulated microwave fields, pulsed magnetic fields, and electric fields (5-7). The discussion of data in this manuscript will be confined to experiments involving a field of 450 MHz, amplitude-modulated at low frequencies.

<sup>\*</sup> This paper was updated in September 1994.

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### MATERIALS AND METHODS

Field exposure, which employed a Crawford cell exposure system, was operated in the same general configuration as described in detail (5,6). The cell was designed to operate as a coaxial transmission line with a characteristic impedance of 50 ohms a spectrum of frequencies. With biological test specimens or cell culture dishes in place, a 50-ohms non-inductive termination standing wave ratio (SWR) did not exceed 1.17:1 at the operating frequency of 450 MHz. Cell viability was not altered by exposure to any of the fields used in the studies presented here. A field-generating system comprised of low-frequency waveform generator served as a modulating signal source. This signal was applied through a PIN diode modulator with an output of a 450 MHz phase-lock loop controlled signal generator. The generator drove a broad band linear power amplifier with a maximum power of 20 W. Depth of sinusoidal amplitude modulation was monitored with an oscilloscope and with an in-line modulation meter/forward reflected power meter. Modulation depth was maintained at 75 to 85%. An input of 1.7watts peak envelope power (PEP) to the cell produced a peak field intensity of 1.0 mW/cm<sup>2</sup>. PEP levels were adjusted to this level with a carrier wave modulated to a depth of 75 to 85% in all experiments. The SAR under these exposure conditions was 0.08 W/kg. The Crawford cell was housed in a large incubator maintained at 37°C. Temperature changes after equilibration and during field exposures were typically around  $\pm 0.1^{\circ}$ C. Exposed culture dishes were maintained in a similar humidified plexiglass box in the same incubator placed outside the Crawford cell. Cultures of Reuber H35 hepatoma cells and the other cells described were maintained under standard culture conditions as described in detail (6-9).

Measurement of ODC activity occurred in supernatant preparations made from cells following exposure at the indicated times to the field. ODC activity is represented as the amount of <sup>14</sup>CO<sub>2</sub> from 0.25  $\mu$ Ci[<sup>14</sup>C]L-ornithine during a 60-minute incubation of the supernatant under control conditions at 37°C at a total ornithine concentration of 0.2 mM (see reference 8 for details).

Total RNA isolated method Chomczynski was using the of and Sacchi (acid/guanidinium/phenol/chloroform) (10) and resuspended in 10 mM tris buffer, pH 7.5. Twenty µg of the total RNA was added to a microfuge tube containing formaldehyde and then denatured by boiling for 1 minute before being loaded onto a 1.1% agarose gel. After electrophoretic separation, the RNA was transferred to a nylon membrane using a vaccublot (IBN) vacuum transfer apparatus. The membrane was then vacuum baked and placed in a bag along with 20 ml of rapid hybridization buffer (Amersham) and incubated at 65°C for one hour. After prehybridization was complete, 10 million CPM of a random-primer <sup>32</sup>P-labelled ornithine decarboxylase probe (specific activity > 2 x  $10^9$  CPM/µg) was added to the bag to hybridize for 3 hours at 42°C. When hybridization was complete, the filter was washed in 0.2 X SSC to remove the nonspecifically bound probe. The washed filter was then subjected to autoradiography at 70°C for 48 hours. After processing the film, only the bands corresponding to ODC mRNA were clearly visible. The autoradiograph was scanned with a densitometer and the density of the bands compared as an indication of the relative amounts of ODC mRNA present in the various samples. Polyamine concentrations in the culture media of cultured cells were determined as described in detail in reference 11.

For all the experiments illustrated in Figures 1, 2 and 3, the cultured cells were exposed to the field for a 1-hour period after which they were removed and assayed at the times indicated. In Figure 4, the effects of field exposure upon the amount of putrescine exported in the culture media is analyzed. In this case, the cells were exposed continuously to the amplitude-modulated microwave field.

#### RESULTS

The effects of a 1-hour exposure of Reuber H35 hepatoma cell culture and 294T human melanoma cell culture to the 450 MHz field amplitude-modulated at 16 Hz for a period of 1 hour is illustrated in Figures 1a and b. During the 1 hour of field exposure the activity of ODC can be observed to increase



Figure 1b

from a value of 20 pmoles  $CO_2/mg$  protein per hour x  $10^{-2}$  to a value of 30, an increase of approximately 50%. At time 0 the cells were removed from the field and assayed for an additional 3-hour period as illustrated. The activity of ODC in the field exposed cells can be observed to remain elevated during the 3-hour period subsequent to field exposure. A similar early effect of field exposure was observed in the 294T human melanoma cells. Following 1-hour exposure to the field the activity of ODC was observed to increase by approximately 50% as shown by the 0 hour value. The activity of ODC in these cells remained elevated for only a 1 hour period after being removed from the field whereupon they return to the control or sham field values illustrated by the solid circles and solid lines.

The effects of the frequency of the amplitude modulation upon the ability of RF field to induce increases in ornithine decarboxylase activity is shown in Figure 2. In these experiments the Reuber H35 hepatoma cells were placed in the field for a 1-hour period and assayed immediately upon removal from the field, i.e., comparable to the time 0 points shown in Figure 1. The data is shown relative to the



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control value of ornithine decarboxylase observed in the unmodulated 450 MHz field shown as the crosshatched bar. It is apparent that only low-frequency amplitude modulated 450 MHz fields were capable of altering the activity of ornithine decarboxylase in these cells. Amplitude modulation frequencies of 12, 16 and 20 Hz produced increases in ornithine decarboxylase activity in this system. The unmodulated and higher modulation frequencies were without effect.





A number of investigators have reported that 60 Hz magnetic fields as well as pulsed magnetic fields of a variety of nature were capable of inducing alterations in eukaryotic gene expression (12-14). In addition, it has been known for many years that many of the stimuli which lead to an increase in ornithine decarboxylase activity inside of cells increased the level of messenger RNA specific for ODC under these conditions (15). For these reasons, we investigated the ability of 16 Hz modulated microwave field to lead to alterations in the mRNA for ODC. The Reuber H35 hepatoma cells were exposed for a

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1-hour period to the field and assayed for the presence of ODC mRNA at the times indicated as described in the materials and methods. For these experiments, triplicate samples were analyzed by Northern gel analysis and the autoradiograms scanned with a densitometer. The data is represented relative to the amount of ODC mRNA observed in control or sham exposed cells. As can be seen in Figure 3, the same field exposure which resulted in an increase in ODC activity did not cause any change in the relative amount of mRNA specific for ODC in these cells throughout a 4-hour post-exposure period. We have additionally analyzed for the amount of ODC mRNA produced during the exposure to the field, i.e., -1 hour to 0 hours and also have observed no increase in ODC mRNA relative to control values (data not shown). Under these identical culture conditions the phorbol ester derivative TPA led to an 8-fold increase in ODC mRNA within a 4-hour period, and insulin causes an 11-fold increase within an 8-hour period (data not shown).

Recently our laboratory has begun to explore the phenomenon of putrescine export or efflux from the inside of the H35 cells to the outside (16). We have recently characterized a transport system present in most eukaryotic cells which is capable of transporting putrescine from the inside of the cell to the outside of the cell in a highly regulated manner. We wished to determine whether exposure to low-energy electromagetic fields would effect this important parameter in the regulation of polyamine metabolism and ODC activity. We continuously exposed the H35 cell cultures to the 16 Hz amplitude-modulated microwave field  $\pm$  TPA as described in Figure 4. After 5 hours the cells receiving TPA showed significantly more putrescine exported into the culture medium than did the cells not receiving TPA. Exposure to the field had an inhibitory effect on the constituitive level of putrescine export in control cells and upon the TPA-stimulated export process.

EFFECT OF MODULATED RF FIELD ON PUTRESCINE EXPORT



Figure 4

#### DISCUSSION

Exposure of cultured cells to athermal levels of amplitude-modulated 450 MHz fields led to a significant and long-lasting (relative to the exposure time) increase in the intracellular enzyme ornithine decarboxylase. Even a transient 1-hour exposure to the field resulted in a longer than 4-hour elevation in ornithine decarboxylase activity (Figure 1). The ability of the 450 MHz microwave field to induce ornithine decarboxylase activity in this cell system furthermore depended upon the frequency of the amplitude modulation (Fig. 2). The microwave carrier wave alone was ineffective in leading to a change

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in activity, with the maximum degree of enhancement of enzyme activity occurring with an amplitude modulation of 16 Hz.

Many laboratories have now observed increases in the enzyme ornithine decarboxylase in cultured cells following exposure to a variety of electromagnetic fields (Table 1) (18-22). At least six separate laboratories have observed changes in ODC activity comparable to what is reported here when monolayer cultured cells were exposed to a number of ELF exposure paradigms including pulsed electromagnetic fields, amplitude modulated 450 MHz fields, 60 Hz electric fields, and 50-65 Hz electromagnetic fields. The general observations made by all these investigators was that: only relatively "low-energy athermal fields" were required to cause these changes in this enzyme, only a reasonably short (in the hour range) time of field exposure was required to change the activity of the enzyme and there was a variety of cell types that were sensitive to field-mediated changes in ODC activity. For these reasons, changes of ODC activity following field exposure could be used as a convenient "marker" for assaying the "field responsiveness" of a given cell or tissue. By using changes in ODC activity as an endpoint, various combinations of frequency, dose, time, magnetic vs. electric parameters, could be interrelated in terms of defining which aspects of ELF exposure are the most critical and important in terms of causing cellular responses. Taken in total, the results described in Table 1 alone argue persuasively that mammalian cells are capable of sensing and responding to "low-energy" ELF.

# Table 1Studies Reporting Alterations in Ornithine DecarboxylaseActivity Following ELF Exposure in Cultured Cells

Authors	Field	Cell Type
Somjen et al, 1983 (18)	pulsed electric field	primary bone cells
Cain et al., 1985 (19)	pulsed magnetic field	primary bone cells
Byus et al., 1985 (5)	AM, 450 MHz	H35 hepatoma, 294T melanoma
Byus et al., 1987 (6)	60 Hz electric field	H35 hepatoma, CCM, P3
Litovitz et al., 1991 (20)	55 and 65-Hz EMF	L929 fibroblasts
Mattson et al., 1992 (21)	50 Hz EMF	HL-60
Cain et al., 1993 (22)	60 Hz EMF	C3H/10T 1/2 fibroblasts

The molecular mechanism responsible for the ELF induced alterations in ODC activity appear not to involve any transcriptional events. In the data presented here, Figure 3 and in reference 21, ELF exposure which caused consistent reproducible changes in intracellular ODC activity failed to alter the level of ODC-specific mRNA in these cells. Current data indicate that a highly significant mechanism for the rapid and marked changes in intracellular ODC activity involve polyamine-mediated stimulation or modulation of ODC degradation potentially involving another protein and termed the "ODC antizyme" (23). It is believed that changes in product polyamine levels feedback through at least one other protein to lead to the inhibition/degradation of ODC protein controlling the amount of polyamine produced at any given time (4).

For this reason we believe that our recent observations concerning the ability of the low-frequency amplitude-modulated RF field to significantly alter the export or efflux of putrescine from the cell (Figure 4) may offer an attractive hypothesis for further investigation concerning the mechanisms involved in field mediated stimulation of ODC activity. By effecting the amount of putrescine which is present inside the cell, field exposure could profoundly influence the activity of ornithine decarboxylase by regulating the rate of degradation of this enzyme. We are concentrating our efforts on understanding the role that putrescine export plays in the regulation of ODC activity, and characterizing the molecular nature of this export system more fully so that we can investigate the specific manner in which ELF interacts with the export system.

Does the observation that ELF causes changes in ODC activity in many different cell types allow a better understanding of any potential deletory health effects of ELF exposure in the human population? This is a very difficult and very important question. In terms of the cancer process as studied in a variety of animal models, changes in ornithine decarboxylase activity have been linked to the "promotion" phase of tumorigenesis by a number of investigators (24-26). Increases in ODC activity in animal tumor models have been shown to be essential but not sufficient for the tumorigenic process (25). A point of interest is that normally during the process of tumor promotion induced by various chemicals, the changes or increases in ODC activity which are observed are of a considerably greater magnitude than what has been observed for ELF-induced ODC changes. However, it is difficult to establish meaningful dose-response relationships between ODC activity changes and tumor incidence using promotional chemicals in animal models, particularly at the extremely low end of chemical treatment and ODC induction.

Does the fact that low-energy ELF exposure leads to changes in ODC activity mean that field exposure is serving as a tumor promoting stimuli in the cell or tissue being observed? This question can not be answered with the current information at hand.. There are many examples of chemical stimuli which will change ornithine decarboxylase activity yet do not serve as a tumor promoting stimulus (25). Detailed experiments must be performed to assess the appearance of tumors or a transformation phenotype using promotion and co-promotion protocols in order to determine the promotional activity of field exposure in relation to ODC activity. Recent experiments in the mouse model of epidermal carcinogenesis, a model where polyamines have been shown to be essential for tumorigenesis, have shown a potential copromotional effect of 60-Hz magnetic fields (27-28). Statements suggesting that there can be no "effects" of ELF exposure are arguably incorrect.

Further research into the molecular biophysical mechanisms of field, cell, and tissue interactions, a better understanding of the basic science involved in the process of transformation, studies using tumor endpoints involving promotion and co-promotional effects of ELF field exposure in animal models, and further studies of an epidemiological nature, will all be necessary to provide an accurate health risk assessment for environmental effects of electric and magnetic field exposure. Unfortunately, given the complex nature of these phenomenon, such answers will not be forthcoming in a short period of time. However, these questions will ultimately be answered if not ignored.

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D. ABSTRACT. On April 26 and 27, 1993, the U.S. Environmental Protection Agency (EPA) Office of Air and Radiation and Office of Research and Development held a conference to assess the current knowledge of biological and human health effects of radiofrequency (RF) radiation and to address the need for and potential impact of finalization of federal guidance on human exposure to RF radiation. More than 200, people attended the conference. Attendees represented the federal government, academia, the private sector, trade associations, the media, and the public. Plenary papers presented at the meeting focused on current research findings on a variety of topics, including exposure assessment, dosimetry, biological effects, epidemiology, the basis for exposure limits, and emerging health issues. Panel discussions focused on identifying key scientific information needs for and the policy implications of the development of further EPA guidance on human exposure to RF radiation. The policy of the development of further EPA guidance on human exposure to RF radiation. The policy involves a record of much of the information presented at the conference, outlines key recommendations provided to EPA by conference participants, and presents the EPA strategy for addressing RF radiation. Volume 2, antergraphic and provides the plenary papers presented by invited speakers. Two key conclusions emerged from the conference: (1) there is sufficient information on thermal exposure/effects on which to base an RF radiation exposure to RF radiation and to develop a longer term strategy to address remaining issues. Part of this strategy has involved creating an inter-agency work group and requesting the National Council on Radiation Protection (NCRP) to assess several remaining issues. Information provided at the conference also was used as a basis for EPA comments to the Federal Communication commission (FEC) 1993 proposal to adopt the RF radiation exposure guidelines developed in 1992 by the American National Standards Institu					
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