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ORIGINAL ARTICLE

A need to provide explanations for observed biological effects of radiofrequency exposure

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Abstract

Although there is scientific consensus that radiofrequency (RF) exposure at high intensity can cause thermal effects, including well-established adverse health effects, there is still considerable controversy on whether low-intensity RF exposure can cause biological effects, especially adverse health effects. The objective of this paper is to describe several reported "non-thermal" effects that were later shown to be due to a weak thermal effect or an experimental artifact by properly conducted and thorough follow-on scientific research. First, the multiple factors that can cause different RF energy absorption in biological tissues are reviewed and second, several examples of experimental artifacts in published papers are described to demonstrate the importance of paying attention to dosimetry and temperature control. For example, isolated nerve response studies show that when temperature of the RF-exposed tissues is controlled, effects disappeared. During RF exposure, conductive electrodes routinely used in physiological studies have been shown to cause field intensification at the tips or contacts of the electrodes with biological tissue; thus, the RF exposure at the site of measurement could be much higher than the incident field. In some *in vitro* studies, a lack of temperature uniformity in RF-exposed cell cultures and rate of heating explain changes originally reported to be due to low-level RF exposure. In other studies, detailed dosimetry studies have identified artifacts that explain the reasons why so-called "non-thermal" effects were mistakenly reported. Researchers should look for explanations for their own findings, and not expect others to figure out what was the reason for their observed effects.

Keywords

Artifacts, dosimetry, exposure systems, mechanism, non-thermal effects, thermal effects

History

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Introduction

Radiofrequency (RF) safety concerns started in the 1950s with exposure to radar, then expanded to radio and TV broadcasting in the 1960s, microwave ovens in 1970s, police radar in 1980s and mobile phones and other wireless communication devices in the last 20+ years. These concerns can be addressed by the weight-of-scientific evidence in approximately 3000 peer-reviewed articles in the IEEE database (http://ieee-emf.com/) relating to RF bioeffects that includes more than 1300 peer-reviewed papers on mobile telephony exposure. The extensive RF publications (in addition to those included in the IEEE database) have been used by both the International Commission on Non-Ionizing Radiation Protection (ICNIRP) and International Committee on Electromagnetic Safety (ICES) of IEEE to develop exposure limits to protect against established adverse health effects. World Health Organization (WHO) in its Fact Sheet 193 has listed the ICNIRP guidelines and the IEEE ICES standard, thus indicating the importance of exposure standards that are based on reviews of the peer-reviewed literature including both high and low RF exposure levels (WHO, 2014). However, reports of effects at low exposure levels continue to raise public concerns about the safety of current RF exposure limits. Because there is no known mechanism to explain any observed effect at low exposure levels, the changes have been called ''non-thermal effects'' by some researchers. The problem in confirming that the effect is indeed ''non-thermal'', and not due to an experimental artifact or a small change in temperature, contributes greatly to the controversy about bioeffects of RF exposure. Labeling a biological response as a ''non-thermal effect'' implies that the effect is due to a ''yet-to-be-discovered'' mechanism other than a temperature increase. The objective of this paper is to show the importance of properly conducted and thorough scientific research in identifying a weak thermal effect or experimental artifact as an explanation for a number of biological changes supposedly due to a ''non-thermal'' effect of low-level RF exposure.

Factors affecting dosimetry

In a tutorial paper, Chou et al. (1996) have discussed the following factors that affect dosimetry.

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Dielectric properties

The magnitude and spatial distribution of EM fields within biological tissues depend on the dielectric properties of tissue (dielectric constant and conductivity), which are dominated by the water content. Therefore, tissues can be divided into those with high water content, such as eye, muscle, skin, liver and kidney, and those with low water content, such as fat and bone. The dielectric constant and conductivity of tissues vary over a wide range and are frequency dependent.

Tissue geometry and size

The highest local specific absorption rate (SAR) is usually at or near the surface of an exposed object. For curved surfaces and ''resonant objects'' high SARs (''hot spots'') exist at various locations. A complex biological system, such as a human or animal body, consists of multiple layers of tissue. Each layer has different dielectric properties and forms an electromagnetic (EM) boundary. When exposed to an RF field, the field propagates within the multilayered object. A portion of the energy is reflected from each boundary, and a portion is transmitted into the next layer. The amount of transmission and reflection at each boundary depends on the difference in dielectric properties of the tissues (characteristic impedance mismatch). Fat thickness, tissue curvature and dimensions of the body, limbs and head relative to the wavelength all affect the energy distribution.

Tissue orientation and field polarization

It has been shown that the SAR in an exposed subject is maximal when the long axis of the body is parallel to the direction of a uniform external electric field. For example, at 10 MHz, energy coupling in a freely moving rat exposed to a constant power density RF field may vary by about 20-fold, depending on the field or body orientation. The ratios are different at other frequencies.

Field frequency

In addition to the frequency dependence of dielectric properties, the strength and spatial distribution of internal fields also vary with frequency. Calculation of the variation of average SAR with frequency for a human-sized sphere showed that, at low frequencies, the average SAR varies as the square of the frequency. At intermediate frequencies, the average SAR increases directly in proportion to frequency and reaches a maximum at the resonance frequency. The local SAR reaches a maximum at a specific frequency, i.e. whole-body resonance. At resonance, the length of the long axis of the exposed body is approximately four-tenths of the field wavelength in air.

Source configuration

In the far field, with the exception of polarization, the SAR is independent of source configuration (there is no interaction or ''coupling'' between the source and the object). However, in the near field, energy coupling depends on the source shape and size, e.g., an operator's position relative to an RF dielectric heater or heat sealer.

Exposure environment

The quantity of energy absorbed by a body in an RF field depends on environmental factors, which include whether the subject is exposed in free space, on a ground plane, near metal reflectors, or in an electrically conductive structure, such as a resonant cavity or waveguide. The presence of objects in the field, such as other animals in the same cage, can also cause SAR variation in an individual animal due to scattering of energy by the other animals. Nose or mouth touching can induce hot spots at contact points due to highly induced current between animals. Metal implants can cause intensification and modification of SAR patterns within tissue. Electric field intensification at the tip of a metal electrode is dependent on its length and diameter as well as the polarization of the RF field.

Time-intensity factors

External field intensity and exposure duration are important parameters that determine the total energy absorbed by tissues. When an RF field is amplitude or pulse modulated, SAR also varies with time. Therefore, measurement of the time-averaged SAR in itself is not adequate for exposure characterization; thus, the modulation characteristics must be specified when relating the SAR to any observed effect. Also, SARs vary with the animal's position when exposed to RF fields. Therefore, when an animal moves, the SARs change as a function of time.

Examples of artifacts

Some of the examples have been shown previously (Chou, 2003). Interested readers can find more details in that paper. As mentioned, the objective of this paper is to show how studies of temperature control and dosimetry have been helpful in identifying reasons why some biological changes were mistakenly reported to be ''non-thermal'' effects.

Isolated nerve response

In the 1960s, a Soviet scientist, Kamenskii (1964) reported that isolated nerves exposed in a waveguide showed significant effects on nerve excitability and action potentials. Although temperature measured with a thermocouple at the surface of the small nerve in the middle of the waveguide showed no measurable temperature rise, our studies found this effect to be due to artificially high absorption in the isolated nerves exposed in air and parallel to the E-field, especially near the waveguide walls. When the nerve was kept in a temperature-controlled waveguide filled with physiological solution, no effect on action potentials other than thermal in origin was observed, even if exposed to very high power levels with peak SAR up to 220 kW/kg (Chou and Guy, 1978). The effects in the original Soviet study were due to the particular *in vitro* exposure condition. When the proper temperature control was applied, the effects disappeared.

Highly conductive electrodes

The use of conventional 3 M KCl glass electrodes for excitable cell recording and tungsten electrodes for neurophysiological studies is a common practice. However, when used in RF fields, the enhanced electric field at the tip of the electrodes can create severe problems. This is similar to putting a metallic rim glass cup inside a microwave oven and starting the oven. Excessive field intensification at the metallic rim can cause smoke, fire and glass breakage. Thermograms showed that the rate of energy absorption at the tip of the tungsten electrode is increased by more than 50 times in a cat brain exposed to 915 MHz fields (Johnson and Guy, 1972). High resistance leads have been shown to minimize RF pickup and reduced field concentration at the electrode tips. Angelone et al. (2010) did a comprehensive volumetric assessment of changes in the RF field with and without metallic EEG leads and showed an increase of two orders of magnitude in single-voxel power absorption in the epidermis and a 40-fold increase in the brain during exposure to the 915 MHz mobile phone. This enhancement confirms the validity of the question whether any observed effects in studies involving EEG recordings during RF-field exposure are directly related to the RF fields generated by the source or indirectly to the RF-field-induced currents due to the presence of conductive EEG leads. Regrettably, metal electrodes are still being used today for EEG recording to study mobile phone effects on EEG.

In a hyperthermia experiment, a 27.12 MHz capacitive field exposure system was used to heat a pig to 42 °C (rectal temperature). The pig ear where the intravenous (IV) drip was inserted got a severe burn (Figure 1). This was caused by the excessive heating of conductive solution in the thin IV tube. In a similar condition (Testylier et al., 2002) where the electric field was parallel to the IV drip to a rat, the investigators incorrectly concluded that the observed effects were due to low level RF fields (Figure 2). There is another mistake in Testylier et al.'s study (2002) because the SAR was calculated using the external E field and not the internal field in the exposed tissue.

Tattersall et al. (2001) published a paper claiming low-intensity RF exposure caused effects on electrical activities in hippocampal slices of rats. After many years of dosimetry studies and with an improved exposure system, Tattersall reported ''Electrode-induced heating artifacts in brain slices exposed to RF fields'' in 2007 at an IEEE committee meeting in London. Figure 3 shows the different results when a new exposure system was used to expose the brain slices. In the new system, no effect was observed at 29 mW/kg, whereas effects have been reported at 4.5 mW/kg in the old system.

Low-level behavioural effect

In the 1960's, there was a study in the US (Korbel and Thompson, 1965) that showed behavioral effect in rats at a low power density level, i.e., 1 mW/cm^2. Using models of a rat in a similar cavity and one model with a tongue touching the water bottle and legs and tail on the copper mesh ground, thermograms showed intense hot spots at these contact locations (Guy and Korbel, 1972). At the SAR level (up to 185 W/kg at the hind leg), hyperthermia was expected which explained why the rat behavior was altered. Without these detailed dosimetry data showing that the high local SAR can cause a thermal effect, the 1 mW/cm^2 behavioral effect on the rats was misinterpreted as evidence of a low-level RF effect.

Temperature control problem

A coaxial line system was designed for exposing cells to broadband RF fields (0–100 MHz). The cells were placed inside a 5-ml coaxial cylinder with a stainless steel center conductor and outer conductor and a Teflon bottom. The

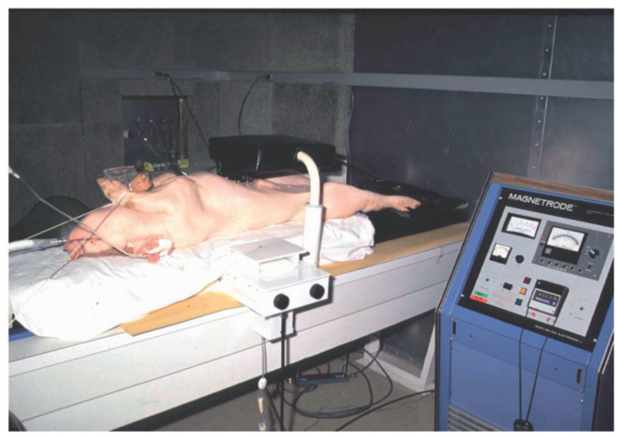

Figure 1. A hyperthermia experiment exposing a pig to 27.12 MHz E-fields to induce whole body heating. The IV tubing for anesthetics caused severe burn at the ear due to RF induced current [Study coducted by C-K. Chou at the City of Hope].

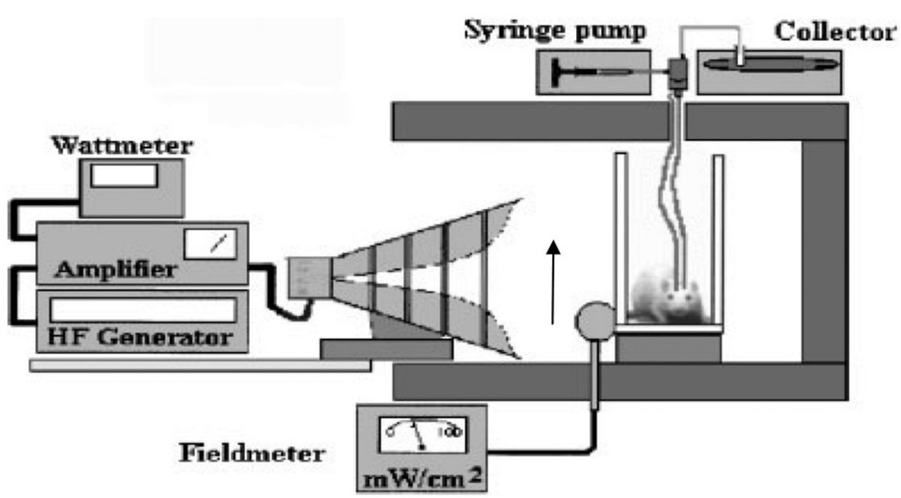

Figure 2. Setup used by Testylier et al. (2002) showing IV tubing parallel to the E field (indicated by the vertical arrow). Also incorrectly used externally measured E-field to calculate SAR in rats.

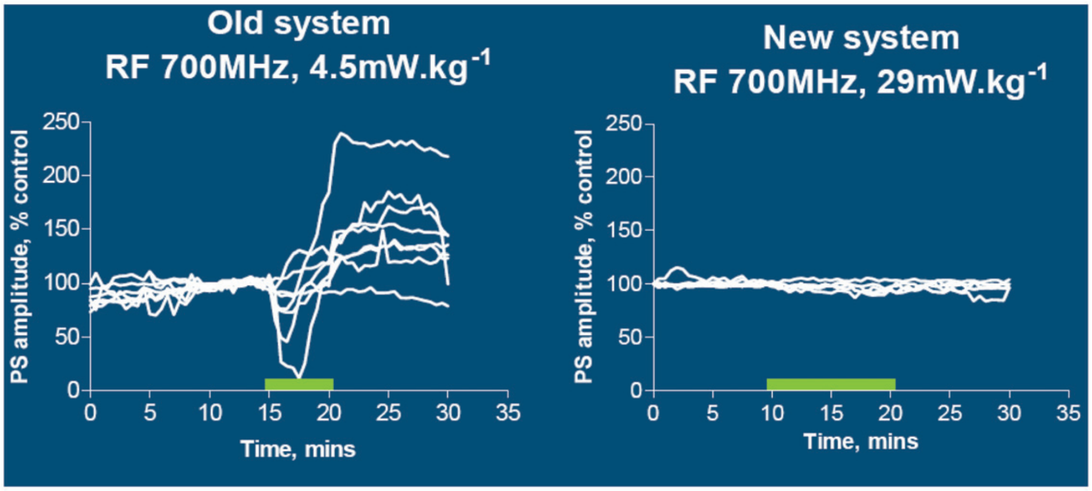

Figure 3. Effects shown on the left were verified to be caused by a metallic electrode-induced heating (horizontal bar for RF exposure) [John Tattersall IEEE TC95 presentation in London, Minutes of the March 2007 meeting Attachment 8, http://www.ices-emfsafety.org/meetings_archive.php].

container for the cell culture was surrounded by a circulating mineral oil bath to keep the culture temperature constant. The temperature variation of the culture medium, which was monitored by a single non-perturbing Vitek™ (BSD Medical Corporation, Salt Lake City, UT) temperature sensor, was less than 0.2 °C. While this result indicated that the culture temperature was relatively constant at one location, additional work identified a problem with the experiment that led to the reporting of an artifactual biological effect. This puzzling effect was resolved after a circulating tube connected through a pump was connected to the 5-ml cup to circulate and stir the cells, so that they would not sink to the bottom of the cup. When cells stayed at the Teflon® bottom, there was a thermal gradient due to the cooling of the bottom. With a higher intensity RF field, a cooler circulating temperature was needed to keep the culture at a constant temperature, and a higher thermal gradient was formed at the walls and the bottom. After the stirring, the effect disappeared. This experiment signifies the importance of precise temperature control at the cell locations.

In 2003, my colleague and I visited Tel-Aviv University to observe an experiment, which researchers claimed to have found RF non-thermal effects on cells. We inserted non-perturbing temperature sensors in the exposed flask, and a 4 °C temperature gradient was found in the culture media. Against our recommendation, the paper was submitted and got published in the Bioelectromagnetics Journal (Mashevich et al., 2003). The paper received the second place award for the most influential journal paper in 2008. As pointed out in our comment of the paper (Chou and Swicord, 2003), RF heating and conventional conduction heating are different. Comparing the final temperature in tissues or cells does not necessarily equate the two types of heating, because the different rates of heating and thermal gradients are difficult to match identically. One can verify that an effect is thermal by controlling temperature, but if the effects are not identical, one still cannot conclude that the effect is non-thermal because of the differences in both temporal and spatial heating profiles. This is illustrated in another paper (George et al., 2008) in which the authors claimed a non-thermal effect because microwaves cause a significantly higher degree of unfolding than conventional thermal stress for protein solutions heated to the same maximum temperature. The two heating conditions are not comparable. The heating rate caused by microwave exposure is much higher than that from a water bath. Furthermore, the heating durations are different.

De Pomerai et al. published a paper in 2000 in *Nature* reporting microwaves cause non-thermal effects, but the paper was retracted in 2006 (de Pomerai et al., 2006). With more detailed dosimetry studies, the team published a follow-up paper in 2009 and reinterpreted it as a subtle thermal effect caused by slight heating (Dawe et al., 2009). Without continued efforts to explore why there was a non-thermal effect, it would have remained in the literature as another evidence of a ‘‘non-thermal’’ effect.

Conclusions

The history of bioelectromagnetic research shows that claims for a number of ‘‘non-thermal’’ effects have proved to be unwarranted because the experimental approach was not sufficiently robust to determine the possible influence of a small change in temperature or experimental artifacts. A positive effect must be explained with a mechanism. What is the reason of the observed effect? Is the effect directly caused by the fields or indirectly caused by the fields. Reporting a ‘‘non-thermal effect’’ does not complete the scientific study, i.e., ‘‘I don’t know what caused the effect, but it is not due to heating’’. Researchers should look for explanations for their findings as did Tattersall and de Pomerai. Because of the complex interaction between RF fields and biological systems, researchers must include detailed and accurate dosimetry as an integral part of their biological studies to make their efforts useful for the understanding of RF bioeffects. At this time, although there are a number of reported ‘‘non-thermal’’ RF effects, none are confirmed to be associated with adverse health effects, as deliberated by the IEEE, ICNIRP and WHO.

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Declaration of interest

The author's own studies mentioned above were conducted at the University of Washington, City of Hope National Medical Center and Motorola. Currently the author is retired. The author reports no conflicts of interest. The author alone is responsible for the content and writing of the article.

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