

HUMAN EXPOSURE TO RADIOFREQUENCY ENERGY: THE NEED TO ENHANCE THE THERMAL RATIONALE

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100-Word Summary

Existing limits for human exposure to radiofrequency (RF) energy as developed by IEEE (TC95 of IEEE ICES), ICNIRP, and the NCRP are based upon adverse effects due to temperature (with the exception of cell depolarization with certain signals below ~5-10 MHz and membrane disruption with high peak pulses). Although not dismissing the possibility of “non-thermal” interactions that might be confirmed in future studies, a detailed understanding of precise time-temperature conditions associated with local tissue damage is essential. The tutorial will summarize the outcome of a workshop entitled “Thermal Aspects of Radio Frequency Exposure” held in Gaithersburg Maryland in January 2010 to characterize the state of science regarding tissue-specific time-temperature effects.

2-Page Abstract

Humans use a considerable amount of metabolic and behavioral energy to keep cells at temperatures in balance between facilitating metabolic activity and not overwhelming damage-repair systems^{1,2}. When at rest in our thermal neutral zone (~24-31°C)³ healthy individuals maintain an isothermal core by tight regulation of cutaneous blood flow. When metabolic energy production and/or ambient conditions create a situation of net heat retention, autonomic responses in addition to cutaneous blood flow are initiated. When our thermoregulatory system is overwhelmed by increased energy input and cells are exposed to temperatures that overcome damage repair, there is a time-dependent linear relationship with apoptotic and necrotic death in terms of cumulative minutes at 43°C (CEM₄₃)⁴ based upon Arrhenius principles and protein denaturation⁵. Although all cells demonstrate this linear time-temperature relationship, different cells, tissues, and species have markedly different thermal tolerances⁶.

Internationally recognized limits for human exposure to radiofrequency (RF) energy have been developed by the Institute of Electrical and Electronic Engineers Technical Committee 95 (IEEE TC95)⁷, the International Commission on Non-Ionizing Radiation Protection (ICNIRP)^{8,9}, and the National Council on Radiation Protection¹⁰ based upon adverse thermal endpoints^{*,†,‡}. In an effort to

* The definition of “thermal” in this paper is not the literal physical description of the transfer of a single photon of electromagnetic energy into vibrational or rotational energy of a dipole molecule (e.g., water), but instead the larger-order energy transfer resulting in a detectable increase in measured temperature. It might also be applied to physiologic parameters (e.g., blood flow, sweating) that occur in order to maintain isothermal temperature.

† ICNIRP (1998) quote: “Overall, the literature on athermal effects ... is so complex, the validity of reported effects so poorly established, and the relevance of the effects to human health is so uncertain, that it is impossible to use this body of information as a basis for setting limits on human exposure” and “In general, the effects of exposure of biological systems to athermal levels of amplitude-modulated EMF are small and very difficult to relate to potential health effects”

support RF exposure limit setting efforts, a workshop entitled “Thermal Aspects of Radio Frequency Exposure” was held in Gaithersburg Maryland in January 2010 and co-sponsored by the US Food and Drug Administration and the Wireless Communications Industry. The goal of the Workshop was not to dismiss the issue of “non-thermal” interactions advocated by some researchers and public interest groups, but to better define tissue-specific time-temperature levels for damage. Over 75 individuals participated in the Workshop from the academia, government, the military, and industry.

The goal was to develop consensus on a) the most appropriate health endpoints for a given tissue or system, b) the most appropriate time periods for acute and chronic exposure, and c) well established time-temperature effects. A comprehensive literature review was developed and circulated to the participants prior to the Workshop that analyzed 463 published papers and identified 117 with sufficient thermal characterization for assessment. The output from the Workshop upheld the current rationale and values for *whole body* RF exposure limits and came to the following conclusions regarding tissue-specific time-temperature effects relevant to *localized* exposure limits:

Cardiovascular System

The cardiovascular system is highly responsive to temperature in controlled laboratory¹¹ and environmental settings^{12,13}. Keeping core temperature below $\sim 1^{\circ}\text{C}$ (consistent with WHO [Error! Bookmark not defined.](#), ACGIH [Error! Bookmark not defined.](#), ISO [Error! Bookmark not defined.](#) [Error! Bookmark not defined.](#), and NIOSH [Error! Bookmark not defined.](#)) should allow healthy individuals to maintain normal cardiac output.

Eye:

Modeling studies suggest localized RF exposure at 2 W/kg (general public) and 10 W/kg (workers) might result in temperature increases up to 0.35°C and 1.75°C , respectively. Cornea and lens clouding and protein denaturation in the iris and retina were considered the most relevant adverse endpoints with thresholds of $\sim 40\text{-}42^{\circ}\text{C}$ for ≤ 1 hour from microwave and laser (e.g., ANSI Z 136.1-1993) research.

Skin

Skin temperatures of 38°C ($\sim 100.4^{\circ}\text{F}$) do not trigger significant adverse responses, although 60 minutes at 41°C ($\sim 105.8^{\circ}\text{F}$) can cause transient decreases in procollagen and 60 minutes at 43°C ($\sim 109.4^{\circ}\text{F}$) can also increase matrix metalloproteinases and Hsp70 expression. Little is known regarding the potential adverse stress and aging effects of chronic low-level temperature exposures.

Testes

The traditional endpoint for thermal sensitivity of the testes (decreased sperm count) is transient and time-temperature dependent. Apoptotic cell death in immature spermatocytes and spermatids but not spermatogonia, can be observed in animals at temperatures of $41\text{-}43^{\circ}\text{C}$ for periods of 15 minutes to 1 hour and in humans with at temperature of $1.0\text{-}1.5^{\circ}\text{C}$ above normal¹⁴ for several weeks.

Immune System

[†] IEEE C95.1 (2005) quote: “... the only mechanism of interaction of RF energy ... is thermal ...”

Fever-level hyperthermia (38-39.5°C) can augment the immune response, suggesting (in theory) the possibility that repeated or chronic temperature increases might lead to hypersensitivity reactions or autoimmunity (although no robust evidence has been shown to confirm this).

Nervous system

Significant discussion on whether physiological / pathological endpoints or behavioral / cognitive endpoints represented the most sensitive and relevant measure of neurological damage with no unanimous resolution. Vulnerable cell types in the brain (in order of sensitivity) were presented as endothelial cells, astrocytes, glial cells, and neurons. Blood brain barrier disruption and subsequent tissue damage were associated with temperature elevations ranging from 0.5°C to 4-5°C above core, although this could be significantly influenced by osmolarity, drugs, disease, age, and genetic factors. Challenges in assessing absolute temperature in exposed tissue were a common problem. A CEM₄₃ of 10-17 minutes was proposed as a threshold for cellular damage across the brain, although certain heat shock proteins can be induced at temperatures as low as 38°C for 24 hours. A temperature of ~38.5°C was offered by the group as a level at which the human brain could endure for moderate periods of time without significant damage above background.

Behavior:

Normal brain excursions of 1-3°C above core are associated with normal behavior and activity, while increases of 3-4°C above core for short periods of time can have life-threatening consequences. Changes in behavior generally require core elevations $\geq 2^\circ\text{C}$ for extended periods of time.

Fetal Development

Developmental abnormalities are consistently associated with temperature increases in the mother of 1.5°C for ≥ 1 hour, 2.0 – 2.5°C for ≥ 0.5 -1 hour, $>4^\circ\text{C}$ for ~10-15 minutes. This is highly dependent upon exposure during sensitive developmental stages and in rapidly dividing cell populations. Significant increases in developmental abnormalities would probably not be observed until temperatures ≥ 1 -2°C above core were maintained for ≥ 60 minutes.

Children

Traditional dogma suggest children are more vulnerable to hyperthermia than adults, although recent studies suggest 8-15+yr olds may have a similar capacity to thermoregulate (assuming adequate hydration and comparable intensity of exercise)^{15,16,17}. A preliminary study in 3+ yr olds demonstrated the increased surface / mass ratio can augment the immature thermoregulatory response at temperatures $\leq 37^\circ\text{C}$. A core body temperature of ~39°C (often observed in 8-15+yr olds during activity) was suggested as generally safe for moderate periods of time.

¹ Iliakis et al., DNA double strand break repair inhibition as a cause of heat radiosensitization: re-evaluation considering backup pathways of NHEJ. *Int J Hyperthermia* (2008) 24(1):17-29

² Roti Roti J. Heat-induced alterations of nuclear protein associations and their effects on DNA repair and replication. *Int J Hyperthermia* (2007) 23(1):3-15

³ Gordon CJ. *Temperature and Toxicology: An Integrative, Comparative, and Environmental Approach*. CRC Press, Boca Raton, FL, 2005

⁴ Dewhirst, M.W., et al., Basic principles of thermal dosimetry and thermal thresholds for tissue damage from hyperthermia. *Int J Hyperthermia*, 2003. 19(3): p. 267-94.

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- ⁵ Dewey WC, Diederich CJ, Dewhirst MW. Hyperthermia classic commentary: Arrhenius relationships from the molecule and cell to the clinic. *Int. J. Hyperthermia*, 10:457-483, 1994
- ⁶ Dewhirst M. W., Viglianti B. L., Lora-Michiels M., Hanson M., Hoopes P. J. Basic principles of thermal dosimetry and thermal thresholds for tissue damage from hyperthermia. *Int. J. Hyperthermia*, Vol. 19, Pg. 267 - 294, 2003
- ⁷ IEEE C95.1 – 2005; Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz
- ⁸ International Commission on Non-Ionizing Radiation Protection (ICNIRP) Guidelines for limiting exposure to time varying electric, magnetic, and electromagnetic fields (up to 300 GHz). *Health Phys* (1998) **74**:494 - 522.
- ⁹ ICNIRP, Vecchia P., Matthes R., Feychting M., Saunders R., et al .ICNIRP Statement on the "Guidelines For Limiting Exposure to Time-Varying Electric, Magnetic, and Electromagnetic Fields (up to 300 GHz)". *Health Phys*, Vol. 97, Pg. 257 - 258, 2009
- ¹⁰ National Council on Radiation Protection and Measurements (NCRP) Report 86: Biological effects and exposure criteria for radio frequency electromagnetic fields, (Bethesda, MD) 1-382, 1986
- ¹¹ Rowell LB. Cardiovascular aspects of human thermoregulation. *Circ Res* 1983; 52: 367–79
- ¹² Keatinge et al. *The American Journal of Medicine* Volume 1988;81: 795-800
- ¹³ Donaldson GC et al. *Environmental Research* (2003) 91:1-7
- ¹⁴ Mieusett et al 1987, 1991
- ¹⁵ Inbar O, Morris N, Epstein Y, Gass G. Comparison of thermoregulatory responses to exercise in dry heat among prepubertal boys, young adults and older males. *Exp Physiol*. 2004 Nov;89(6):691-700.
- ¹⁶ Rowland et al. 2007
- ¹⁷ Rivera-Brown et al. 2006