(Thermal) mechanisms of interaction between HF and biological systems

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 thermal aspects of exposure to radiofrequency energy: report of a workshop
Mechanism” is defined by IEEE (2006) as a theoretical formulation that:

- can be used to **predict** a biological effect in humans;
- can be **formulated** in an explicit model using equations or parametric relationships;
- is **supported by data** from humans, or by animal data and can be extrapolated confidently to humans;
- is supported by **strong evidence**; and
- is **widely accepted** among experts in the scientific community.
Mechanism 1
(metric: temperature increase)
Thermal Dependence of Biological Processes
Arrhenius' equation

\[ k = A e^{-E_a/(RT)} \]

- \( k \) = rate constant of a chemical reaction
- \( T \) = absolute temperature (in K)
- \( A \) = pre-exponential factor (or simply the prefactor),
- \( E_a \) = activation energy
- \( R \) = universal gas constant

For most biological systems, \( Q_{10} \sim 2 \) to \( 3 \)
$Q_{10}$ - Practical characterization of temperature dependence

$$Q_{10} = \left( \frac{R_2}{R_1} \right)^{10/(T_2 - T_1)}$$

where

$R$ is the rate

$T$ is the temperature in Celsius degrees or kelvins.

$Q_{10}$ of 2 means that a $10^\circ C$ increase in temperature doubles the reaction rate

Typical range 1.5-3
More sensitive systems exist:

Membrane conductance of TRPV4 channels
“TRPV4 is a functional temperature-sensing channel in native endothelium”

Fun Fact

de Pomerai et al. (2000, 2006) reported induction of heat shock proteins in the nematode *C. elegans* after extended (2 to 24 h) exposures to microwave energy.

This effect was eventually found to be associated with a small (0.2°C) temperature increase in the irradiated samples (de Pomerai et al. 2006).
Relevance to Exposure Guidelines

• Arrhenius equation says that *any* temperature change will produce biological effects
  – some may be adaptive or not adverse to health
  – Some reported “nonthermal” effects might be thermally induced after all

• But... difficult to extrapolate to low exposures (no data)
Mechanism 2
(metric: temperature increase)

Thermal Damage

\[ \frac{d\Omega}{dt} = A \exp \left( \frac{-E_a}{R_b T(t)} \right) \]
\[ \Omega = \int_0^T A \exp \left( \frac{-E_a}{R_b T(t)} \right) dt \]

\( \Omega \) is the thermal damage index

**Isoeffect dose cumulative equivalent min 43 (CEM43)**

\[ CEM43 = \Delta t R^{43-T_c} \]

\( R = 0.25 \) for \( T < 43 \) C

\( = 0.5 \) for \( T > 43 \) C
proximate ranking of thresholds for thermal damage of various tissues. Adapted from a figure c
Fun Fact
Tissues can sustain high temperature increases for short time periods
Gaps in Knowledge

- Data for thermal injury very scattered, not collected using consistent protocols
- Most data at thermal exposures far above safety limits
- Little (no?) basis to extrapolate to low thermal exposures.

Relevance to Guidelines

Nil unless limits are raised considerably
Mechanism 3
(metric: time rate of change of temperature)

Microwave Auditory Effect/Thermoelastic expansion

\[ P_0 = \frac{c_s \beta R \rho S}{C J}, \]

Po = sound pressure
R is the diameter of the heated region
S is the SAR in the exposed region,
\( \beta \) = volumetric thermal expansion coefficient of the tissue, \( c \) = velocity of sound
C is the heat capacity of the tissue, and J is the mechanical equivalent of heat.
Microwave auditory effect

- Typical pulse intensity W/cm², µs pulses

Implications for Guidelines

Threshold hearing phenomenon - no apparent hazard.

Might be considered as an annoyance
Mechanism 4
(metric: time rate of change of temperature)
Thermally-induced membrane depolarization

High dT/dt will affect membrane activity (Wachtel)

Very high peak SAR’s needed (tens of W/kg)

Not relevant to exposure limits
WHENCE 6 MINUTES?

“Our early C-95.4 Committee needed to recommend a time constant. My suggestion was 0.1 h. I was trying to come up with a number with as few significant figures as I could, considering the precision of what we were dealing with. A minute was too short — an hour was too long. But, alas, 0.1 h turned into 6 min, and 6 min implies an accuracy beyond the art…”

SAR Incident power density

Energy Penetration Depth, cm

- Skeletal Muscle
- Brain (White Matter)
- Cornea
- Wet Skin

Frequency, Hz

10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1}
Heating of Tissues by Microwaves: A Model Analysis

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Appendix by Thomas S. Ely\(^4\)

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Pennes’ Bioheat Equation (1948)

\[ k \nabla^2 T - \rho_b \rho_t C_b m_b T + \rho_t \text{SAR} = C_t \rho_t \frac{\partial T}{\partial t} \]

- **T** = tissue temperature
- **k** = thermal conductivity of tissue (0.4 W/m °C)
- **SAR** = microwave power deposition rate (W/kg)
- **C_b** = heat capacity of blood (4000 W sec/kg° C)
- **C_t** = heat capacity of tissue (4000 W sec/kg° C)
- **D_b** = density of blood (1000 kg/m³)
- **D_t** = density of tissue (1000 kg/m³)
- **m_b** = volumetric perfusion rate of blood (40 mL/100 g of tissue per min)
Limiting solutions to BHTE

Early transient period (heat storage term dominates)
\[ \frac{dT}{dt} \bigg|_0 = \frac{SAR}{C_t} \]

Steady state (convection term dominates)
\[ T_{ss} = \frac{SAR}{\rho m_b C} + \frac{k \nabla^2 T}{\rho_b \rho_t C_b m_b} \]
↑ Usually smaller term
Two Time Scales in Bioheat Equation

\[ \tau_1 = \frac{1}{m_b \rho} \approx 60 \text{ sec} \text{ (convection)} \]

\[ \tau_2 = \frac{\rho C L^2}{k} \approx 800 \text{ sec (diffusion, for } L = 1 \text{ cm)} \]

\[ \approx 8 \text{ sec (diffusion, for } L = 1 \text{ mm)} \]

\[ m_b = \text{blood flow} \]
\[ \rho = \text{tissue density} \]
\[ k = \text{thermal conductivity of tissue} \]
\[ L = \text{distance scale of heating (SAR)} \]
\[ C = \text{specific heat of tissue} \]

Shorter time constant dominates
\[ \tau_{\text{eff}} = \frac{T_{ss}}{dT/dt}_0 \] (thermal averaging time)
Green’s function for BHTA

Steady-state spherical

\[ G(R) = \frac{\rho_t}{4\pi k_t R} e^{-R/R_{\text{conv}}} \]

\[ R_{\text{conv}} = \frac{\sqrt{k_t}}{\rho \sqrt{m_b c}} \approx 1 - 2 \text{ cm} \]

\( R = \) distance from center of source
\( R_{\text{conv}} = \) distance scale for convection
\( \rho_t = \) tissue density
\( k_t = \) thermal conductivity of tissue
\( c = \) specific heat of tissue
\( m_b = \) blood perfusion rate
Thermal Response Time and Steady State Temp. Increase in Heated Tissue Sphere (heat conduction only)

<table>
<thead>
<tr>
<th>Radius</th>
<th>Thermal relaxation time, sec</th>
<th>Maximum steady-state temperature increase above surrounding medium, °C (SAR 10 W/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 nm</td>
<td>3.5 ps</td>
<td>$8 \times 10^{-15}$</td>
</tr>
<tr>
<td>10 nm</td>
<td>0.35 ns</td>
<td>$8 \times 10^{-13}$</td>
</tr>
<tr>
<td>1 µm</td>
<td>3.5 µs</td>
<td>$8 \times 10^{-9}$</td>
</tr>
<tr>
<td>1 mm</td>
<td>3.5 s</td>
<td>0.008</td>
</tr>
<tr>
<td>1 cm</td>
<td>350 s</td>
<td>0.8</td>
</tr>
</tbody>
</table>
Bottom Line

• Averaging distance is $\approx 1$-$2$ cm (steady state heating)
  *Thermal conduction is nature’s way of averaging thermal exposure*

• Useful definition of averaging time: steady state temperature increase/ peak SAR

How much precision is needed and at what cost in complexity?
Does ANSI C95.1 Follow Moore’s Law?
Need more features! Cool ideas and technology

Need more...? Fix problems!

Simple Fast Easy to change

Complicated More problems

Incomprehensible Unstable and slow Impossible to change

Kill???

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