Frequency Dependence of Heating Thermal Thresholds for Teratogenicity, Reproduction, and Development, and mm-Wave Exposure to the Skin

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Fundamental mechanism of heating is the same for all the RF frequencies, but:

Penetration is frequency dependent

Distribution of temperature elevation varies

Penetration of mm-waves is limited to skin
Complex Relative Permittivity
\[
\tilde{\varepsilon} = \varepsilon' - j\varepsilon''
\]

where

\( \varepsilon' = \text{dielectric constant} \)
\( (\text{measures polarizability}) \)

\( \varepsilon'' = \text{dielectric loss} \)
\( (\text{measures energy loss}) \)
Dielectric constant $\epsilon_r$

Dielectric loss $\epsilon''$

$\omega_c = \frac{1}{\tau_{macro}}$

$\omega_c = \frac{1}{\tau_{H_2O}}$
Dielectric Dispersion in Tissue

- **Alpha Dispersion**
  - Counterion diffusion effect
  - 100 Hz

- **Beta Dispersion**
  - Capacitive charging of membranes
  - 8 MHz

- **Gamma Dispersion**
  - Dipolar polarization of tissue water
  - 100 GHz
Complex Relative Permittivity

\[ \tilde{\varepsilon} = \varepsilon' - j\varepsilon'' \]

Attenuation Coefficient

\[ \alpha = \frac{\omega}{c} \sqrt{\frac{\sqrt{(\varepsilon')^2 + (\varepsilon'')^2} - \varepsilon'}{2}} \]

Depth of Penetration

\[ \delta = \frac{1}{\alpha} \]
<table>
<thead>
<tr>
<th>Selected Frequency</th>
<th>Skin Depth</th>
</tr>
</thead>
<tbody>
<tr>
<td>MHz</td>
<td>mm</td>
</tr>
<tr>
<td>1</td>
<td>913.0</td>
</tr>
<tr>
<td>100</td>
<td>66.6</td>
</tr>
<tr>
<td>900</td>
<td>30.4</td>
</tr>
<tr>
<td>2.45 GHz</td>
<td>17.0</td>
</tr>
<tr>
<td>30</td>
<td>0.78</td>
</tr>
<tr>
<td>90</td>
<td>0.34</td>
</tr>
<tr>
<td>300</td>
<td>0.23</td>
</tr>
</tbody>
</table>
ANATOMY OF THE SKIN

Epidermis 150 µm

Dermis

94-GHz Penetration Depth

Free nerve ending

35-GHz Penetration Depth
ICNIRP Standard

Basic Restrictions for
100 kHz – 10 GHz Exposures:

Whole Body:
  Occupational  0.4 W/kg
  General Public  0.08 W/kg

Head and Trunk:
  Occupational  10 W/kg
  General Public  2 W/kg

Limbs:
  Occupational  20 W/kg
  General Public  4 W/kg
Specific Absorption Rate (SAR)

For RF Standards:

• SAR is chosen over Power Density because it is a better predictor of Biological Effects

• But not for frequencies greater than 10 GHz, where penetration is limited to skin.
ICNIRP Standard
Basic Restrictions for
10 GHz to 300 GHz Exposures:

OCCUPATIONAL  50 W / m²
GENERAL PUBLIC  10 W / m²
Thermal Thresholds for Teratogenicity, Reproduction, and Development
Thermal Bioeffects

Most sensitive and important irreversible effects occur in:

- Rapidly dividing cells
- Embryo and Fetus
Impact of Thermal Effect

Most Organs
  • Cell death replaced
  • Reversible

Embryo and Fetus
  • Cell death has major Effect
  • Not reversible
HYPERTHERMIA

A Known Teratogen in:

Birds
Hamsters
Mice
Rats
Guinea Pigs
Sheep
Cattle
Non-Human Primates
Arthrogryposis Multiforma
Micrencephaly (%)

Age at Time of Exposure (week of gest.)
# Temperature Duration Thresholds for Fetal Abnormalities

<table>
<thead>
<tr>
<th>Thermal effects</th>
<th>Temp (°C)</th>
<th>Exposure duration (min)</th>
<th>$t_{43}^+$ (min)</th>
<th>Species</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal closure of anterior neuropore</td>
<td>43.0</td>
<td>7.5</td>
<td>7.5</td>
<td>Rat</td>
<td>Walsh (1985b)</td>
</tr>
<tr>
<td>Abortion</td>
<td>40.6</td>
<td>72</td>
<td>2.6</td>
<td>Monkey</td>
<td>Hendrickx et al. (1979)</td>
</tr>
<tr>
<td>Absence of optical vesicles</td>
<td>43.0</td>
<td>7.5</td>
<td>7.5</td>
<td>Rat</td>
<td>Walsh (1985b)</td>
</tr>
<tr>
<td>Absent cerebral cortical plate</td>
<td>43.0</td>
<td>60</td>
<td>60.0</td>
<td>Guinea Pig</td>
<td>Uphold et al. (1986)</td>
</tr>
<tr>
<td>Aqenesis</td>
<td>43.3</td>
<td>60</td>
<td>90.9</td>
<td>Guinea Pig</td>
<td>Edwards (1971)</td>
</tr>
<tr>
<td>Agnathia</td>
<td>43.0</td>
<td>60</td>
<td>60.0</td>
<td>Mouse</td>
<td>Pennycuik (1965)</td>
</tr>
<tr>
<td>Anencephaly</td>
<td>43.0</td>
<td>40</td>
<td>40.0</td>
<td>Rat</td>
<td>Edwards (1968)</td>
</tr>
<tr>
<td>Anophthalmia</td>
<td>40.6</td>
<td>72</td>
<td>2.6</td>
<td>Monkey</td>
<td>Hendrickx (1979)</td>
</tr>
<tr>
<td>Arthrogryposis</td>
<td>42.9</td>
<td>60</td>
<td>52.2</td>
<td>Guinea Pig</td>
<td>Edwards (1971)</td>
</tr>
<tr>
<td>Beak defects</td>
<td>41.0</td>
<td>1440</td>
<td>90.0</td>
<td>Chicken</td>
<td>Nielsen (1969)</td>
</tr>
<tr>
<td>Behavioral abnormalities</td>
<td>41.5</td>
<td>60</td>
<td>7.5</td>
<td>Marmoset</td>
<td>Poswillo et al. (1974)</td>
</tr>
<tr>
<td>Blebbing of cell membrane</td>
<td>43.0</td>
<td>180</td>
<td>180.0</td>
<td>Chin. Hamster</td>
<td>Bass et al. (1978)</td>
</tr>
<tr>
<td>Brain cavitation</td>
<td>40.0</td>
<td>540</td>
<td>8.4</td>
<td>Sheep</td>
<td>Hartley et al. (1974)</td>
</tr>
<tr>
<td>Brain growth retardation</td>
<td>40.0</td>
<td>2880</td>
<td>45.0</td>
<td>Rat</td>
<td>Cockcroft and New</td>
</tr>
</tbody>
</table>
# Normal Rectal Temperatures

<table>
<thead>
<tr>
<th>Animal</th>
<th>Temperature Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baboons &amp; Monkeys</td>
<td>37.0 – 39.0</td>
</tr>
<tr>
<td>Camel</td>
<td>34.0 – 40.0</td>
</tr>
<tr>
<td>Cat</td>
<td>39.0</td>
</tr>
<tr>
<td>Chicken</td>
<td>41.0 – 42.5</td>
</tr>
<tr>
<td>Cow</td>
<td>38.0 – 39.0</td>
</tr>
<tr>
<td>Dog</td>
<td>38.0 – 39.0</td>
</tr>
<tr>
<td>Gerbil</td>
<td>38.5</td>
</tr>
<tr>
<td>Goat</td>
<td>38.0 – 40.0</td>
</tr>
<tr>
<td>Guinea Pig</td>
<td>39.0 – 39.5</td>
</tr>
<tr>
<td>Human</td>
<td>37.0 – 37.5</td>
</tr>
<tr>
<td>Mouse</td>
<td>37.0 – 39.0</td>
</tr>
<tr>
<td>Pig</td>
<td>37.0 – 39.0</td>
</tr>
<tr>
<td>Rat</td>
<td>37.5 – 38.5</td>
</tr>
<tr>
<td>Sheep</td>
<td>39.0 – 39.5</td>
</tr>
<tr>
<td>Sparrow</td>
<td>43.0 – 44.0</td>
</tr>
</tbody>
</table>
Fetal Temperature During Thermal Exposure

Incubator at 43 °C
guinea pig

Core Temperature (°C)

Time (min)

During
After Heat Stress
The thermal equivalent time ($t_{43}$)
is defined mathematically as:

$$t_{43} = \int_{0}^{t_{1}} R^k \left[ T(t) - T_0 \right] dt$$

where:

- $k = (1 \, ^\circ \text{C})^{-1}$, a constant to render the exponent dimensionless
- $T_0 = \text{Reference temperature of 43 } ^\circ \text{C}$
- $T(t)$ = Temperature (which may vary in time) producing the bioeffect
- $t$ = time
- $t_1$ = time required to produce the bioeffect at Temperature $T$
- $R = 4.0$ if $T \leq 43 \, ^\circ \text{C}$
- $R = 2.0$ if $T > 43 \, ^\circ \text{C}$
Abnormalities Occurring below CEM\textsubscript{43} = 1

- Encephalocele in rats
- Exencephaly in mice
- Microcephaly in guinea pigs
- Neural tube defects in mice
- Skeletal malformations in mice and rats
Fetal Developmental Abnormality Thresholds

Temperature Rise

Minutes

CEM_{43} = 1

CEM_{43} = 0.125
## Safe Temperatures For Developmental Abnormalities

<table>
<thead>
<tr>
<th>Temperature Elevation</th>
<th>Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 °C</td>
<td>.25</td>
</tr>
<tr>
<td>5 °C</td>
<td>.5</td>
</tr>
<tr>
<td>4 °C</td>
<td>2</td>
</tr>
<tr>
<td>3 °C</td>
<td>8</td>
</tr>
<tr>
<td>2 °C</td>
<td>32</td>
</tr>
<tr>
<td>1.5 °C</td>
<td>∞</td>
</tr>
</tbody>
</table>
Mitigating Factors in Humans

- Better Thermoregulation
- Fetuses normally are 0.5 °C above core
- Diurnal temperature variation = ~1 °C
- Repair mechanisms may be better
- Enzyme kinetics are driven by absolute temperature not relative temperature
# Temperature Rise From Whole Body SAR

<table>
<thead>
<tr>
<th>SAR</th>
<th>Temp Rise</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 W/kg</td>
<td>4.0 °C</td>
<td>Abnormality</td>
</tr>
<tr>
<td>4 W/kg</td>
<td>1.0 °C</td>
<td>No Harm</td>
</tr>
<tr>
<td>1.5 W/kg</td>
<td>0.4 °C</td>
<td>Safe Level</td>
</tr>
<tr>
<td>0.4 W/kg</td>
<td>0.1 °C</td>
<td>RF Standard</td>
</tr>
</tbody>
</table>

**Note:** Diurnal Variation = ± 0.5 °C
Millimeter Wave Exposure of the Skin
Russian Reported Successes in Millimeter Wave Therapy

- Osteoarthritis
- Esophagitis
- Peptic Ulcer
- Duodenal Ulcer
- Hypertension
- Myocardial Infarct
- Mental Disease
- Rheumatic Disease
- Cancer
- Substance Abuse
- Epilepsy
- Alcoholism
- Psoriasis
- Pain
- Prostatic Hypertrophy
- Anemia
# Ukrainian Clinical Studies

## 1993

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous Diseases</td>
<td>88.7%</td>
</tr>
<tr>
<td>Digestive Diseases</td>
<td>96.1%</td>
</tr>
<tr>
<td>Respiratory Diseases</td>
<td>96.7%</td>
</tr>
<tr>
<td>Mental Diseases</td>
<td>80.3%</td>
</tr>
<tr>
<td>Blood Circulation</td>
<td>92.7%</td>
</tr>
<tr>
<td>“Women’s” Diseases</td>
<td>87.0%</td>
</tr>
<tr>
<td>Skin Disorders</td>
<td>84.8%</td>
</tr>
<tr>
<td>Rheumatic Diseases</td>
<td>84.3%</td>
</tr>
<tr>
<td>Infectious Diseases</td>
<td>96.2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of Centers</th>
<th>325</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>250,000</td>
</tr>
</tbody>
</table>
Millimeter Wave Therapy

• Typical Power Density
  10 – 20 mW/cm²

• “Therapeutic” wavelengths:
  4.9, 5.6, and 7.1 mm
  (frequencies 61.22, 53.57 and 42.25 GHz)

• Exposure of patient’s skin:
  acupuncture points, forehead, occiput
  sternum; big joints, surgical wounds

• 15-30 min session; one session per day; 10-15
  sessions per course
Temperature measurements in the skin during mm-wave exposure with WG opening

Lower forearm

Index finger

Generator G4-141

Frequency: 42.25 GHz
Output power: 52 mW
Effect of Blood Perfusion on Heating

Experimental Techniques
- Vasodilating Cream to increase perfusion
- Blood Pressure Cuff to decrease perfusion
- Laser Doppler Probe to measure perfusion

Exposure
- 208 mW/cm² at 42.5 GHz
- Sites: Forearm and Finger
- Duration: 10 min
Effect of Blood Perfusion on Heating

Results

Forearm $\Delta T = 4.0 \, ^{\circ}C$ by 10 min

Finger $\Delta T = 2.5 \, ^{\circ}C$ by 2 min

Occlusion: $\Delta T = 2 \, ^{\circ}C$ in exposed area

$\Delta T = -2 \, ^{\circ}C$ in unexposed area

Vasodilation: Variable $\Delta T$ depending on Venous pattern
Conclusions:

- ΔT greatly affected by blood flow
- Beam size is important
- Narrow beam
  - Caused shallow and low ΔT
  - Required 2D equations for good fit
- Broad beam
  - Caused deeper and higher ΔT
  - 1D equation provided good fit

Bioheat Transfer Equation

Required \( k_{\text{eff}} = (1 + \beta \cdot f) \cdot k \)
SURFACE TEMPERATURE THRESHOLDS FOR HUMAN OR PORCINE SKIN
(Moritz and Henriques, p. 711, 1947)

![Graph showing surface temperature thresholds for human or porcine skin. The graph includes a curve for epidermal necrosis (2nd degree burn) and a curve for damage threshold (1st degree burn). The x-axis represents exposure time in seconds, minutes, and hours, while the y-axis represents surface temperature in °C.]
HEATING AND PAIN SENSATION PRODUCED IN HUMAN SKIN
BY MILLIMETER WAVES: COMPARISON TO A SIMPLE
THERMAL MODEL

Thomas J. Walters,∗ Dennis W. Blick,∗ Leland R. Johnson,† Eleanor R. Adair,‡ and
Kenneth R. Foster‡

Abstract—Cutaneous thresholds for thermal pain were measured in 10 human subjects during 3-s exposures at 94 GHz
continuous wave microwave energy at intensities up to ≈ 1.8 W cm−2. During each exposure, the temperature increase at
the skin’s surface was measured by infrared thermography. The mean (± s.e.m.) baseline temperature of the skin was
34.0 ± 0.2°C. The threshold for pricking pain was 43.9 ± 0.7°C, which corresponded to an increase in surface temperature
of ≈ 9.9°C (from 34.0°C to 43.9°C). The measured increases in surface temperature were in good agreement with
a simple thermal model that accounted for heat conduction and for the penetration depth of the microwave energy into
tissue. Taken together, these results support the use of the model for predicting thresholds of thermal pain at other
millimeter wave (length) frequencies.
Health Phys. 78(3):259–267; 2000

Key words: skin dose; radiofrequency; radiation, nonionizing; microwaves

Only limited data are available concerning the thermal responses of humans to microwave energy, and most
of those data are for frequencies below 10 GHz. We have measured warmth detection-thresholds across a wide
range of microwave frequencies, including millimeter wavelengths, within the same subject population (Blick
et al. 1997). We have also shown that these thresholds of sensation can be interpreted as reflecting an increase in
surface temperature that is independent of the irradiation frequency (Riu et al. 1997). The use of a standard
protocol that incorporated measurements over a broad frequency range enabled us to determine the importance
of energy-penetration depth both to sensation and to the underlying cutaneous events.

The threshold for thermal pain has been determined for microwave (3 GHz; Cook 1952b) and infrared irra-
diation (Cook 1952b; Hardy et al. 1952) in human subjects. The threshold for pain was found to be a
Warmth Detection Threshold and Penetration Depth: Variation with Microwave Frequency

<table>
<thead>
<tr>
<th>Frequency (GHz)</th>
<th>Threshold (mW/cm²)</th>
<th>Depth of Energy Deposition (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>1</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
<td>10</td>
</tr>
<tr>
<td>100</td>
<td>~200000</td>
<td>~200000</td>
</tr>
</tbody>
</table>

- Warmth Threshold: \( r^2 = 0.978 \)
- Skin Depth: \( r^2 = 0.979 \)
- Infrared Threshold

Microwaves

Infrared
• **First degree burn:**
  - Epidermis is burned;
  - Reddening occurs and swelling is possible
  - Heals without scarring
Second degree burn:
- Epidermis and dermis are burned;
- Intense red discoloring;
- Severe pain, swelling, and blistering.

Third degree burn:
- All layers of skin burned => to fat, muscle, and possibly bone
- May be severe pain, but sometimes extensive nerve damage results in little or no pain
- Areas appear charred black or dry white
- Areas cannot heal fast enough on their own to prevent infection
Pain Thresholds and Safety Margins

- Normal Skin Temperature = 34 °C
- Pain Threshold = 44-45 °C
- First Degree Burn = 55-60 °C
- Second Degree Burn = 60-65 °C
- Third Degree Burn = > 70 °C
Thank You