—————— *ICNIRP Statement* ——————

A CLOSER LOOK AT THE THRESHOLDS OF THERMAL DAMAGE: WORKSHOP REPORT BY AN ICNIRP TASK GROUP

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Abstract—The International Commission on Non-Ionizing Radiation Protection issued guidelines in 1998 for limiting public and occupational exposure to radiofrequency electromagnetic fields (100 kHz to 300 GHz). As part of the process of updating this advice, a 2-d workshop titled "A closer look at the thresholds of thermal damage" was held from 26–28 May 2015 in Istanbul to re-examine the thermal basis of the guidelines and to provide further information on heat-related effects and thresholds of thermal damage. Overall, the workshop provided much useful information relevant to revision of the guidelines. Participants indicated that the effects of heating from radiofrequency fields are consistent with those from other sources, and that the information derived from those studies can be applied to radiofrequency-induced heating. Another conclusion was that absolute temperature of tissues was more important for thermal damage than temperature change. The discussion suggested that the 6-min averaging time used in international guidelines was valid for whole-body exposures but with a large uncertainty: 30 min may be a more appropriate averaging time for localized exposures, and less than 1 min for implanted medical devices. The duration of whole-body radiofrequency exposure is a critical parameter that often determines the effect threshold, but this will be affected by other, ongoing thermoregulation, which is dependant on many factors. The thresholds for localized radiofrequency exposure were difficult to determine because of the potential range of exposure conditions and the possibility of radiofrequency-induced local hotspots. Suggestions for future dose metrics and further research were discussed and are included in this report.
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INTRODUCTION

THE INTERNATIONAL Commission on Non-Ionizing Radiation Protection (ICNIRP) provides scientific advice and guidance on the health effects of all forms of non-ionizing radiation and ultrasound. ICNIRP develops and disseminates such advice through publication of guidelines, reviews and statements, and it also organizes workshops to provide an opportunity to advance the dialogue on non-ionizing radiation protection and to gain expert knowledge about particular areas of science.

ICNIRP produced its most recent guidelines recommending limits of exposure to radiofrequency (RF) electromagnetic fields from 100 kHz to 300 GHz in 1998. These were based largely on avoiding thermal effects of exposure, although it is also important to restrict induced current density in tissues below 10 MHz (ICNIRP 1998). ICNIRP's revision of the guidelines follows the update of the WHO Environmental Health Criteria monograph on RF fields,

as this is part of the overall ICNIRP guidelines setting process. Additionally, ICNIRP decided to review these guidelines as many new studies on the effects of RF fields (particularly from mobile phones) have been published in recent years, and there have been notable advances in computational dosimetry. As part of this process, ICNIRP organized an international workshop, in association with the World Health Organization and the Turkish Ministry of Health, that explored the thresholds for heat-related effects and thermal damage.

That excessive increases in temperature can be harmful to living beings is not disputed. However, there are many uncertainties and gaps in knowledge regarding the thresholds at which increased temperatures (especially those induced by exposure to RF fields) might cause significant localized or whole-body effects. Further, the influence of temperature and humidity of the external environment remain unclear, as do the effects of clothing on thermal responses to RF fields. In addition, the most health-relevant quantity to express the absorbed RF energy, such as specific energy absorption rate (SAR) or thermal isoeffect dose, needs to be considered further. Of particular relevance for exposure assessment are dosimetric considerations of the most appropriate averaging time to use with respect to temperature increase, the mass of tissue involved, and the shape of this tissue.

Overall, the aim of the workshop was to revisit the basic concept expressed by ICNIRP in its previous guidelines that the health-relevant increase of body core temperature was approximately 1 °C and that a whole-body exposure with an average SAR of 4 W kg^{-1} would result in a body core temperature increase of less than 1 °C within 30 min (ICNIRP 1998).

The conclusions from each of the sessions of the workshop are presented here. The program and speakers' presentations are available at www.icnirp.org/en/workshops/article/workshop-thermal-damage.html.

FROM THERMOSENSATION TO THERMOREGULATION

The workshop started with an overview of some of the basic thermal mechanisms. For thermoregulation to occur, it is important that the body senses temperature changes and acts accordingly.

Andreas Flouris (University of Thessaly, Greece) provided an overview of the functional architecture of the thermoregulatory system. There are peripheral and central thermosensors. Detection of temperature is effected by transient receptor potential (TRP) ion channels in pain- and temperature-sensitive neurons. These carry signals to the hypothalamus, brainstem, and insular cortex where thermoregulation is controlled. This can be affected by autonomic and immune responses (that have finite capacity) and by

behavioral responses (that have near infinite capacity). These responses are regulated by different central systems. Autonomic thermoregulation uses vasodilation and sweating to lose heat, or vasoconstriction and shivering to keep and generate heat. From experiments, it appears that behavioral thermoregulation is mainly driven by the skin and not by the body core temperature. Facial temperature and thermal perception are good modulators of behavioral thermoregulation.

Thomas Voets (University of Leuven, Belgium) followed up on this by providing more detail on nerve endings in the skin and the TRP ion channels. There are four types of nerve endings that react differently to different temperatures, which allow the body to respond in an appropriate way: each type of neuron has a different set of TRP ion channels. The calcium influx through these channels not only results in nerve firing but also in release of peptides that may result in a local response such as vasodilation. The ion channels are not only activated by heat but also by everyday substances such as mint, menthol, chili, and capsaicin. There are also differences in the composition of the set of TRP ion channels in different populations, which allow people in warmer climates, for example, to tolerate heat (and chili) better than people in cooler climates. Inflammation makes the TRP channels more sensitive.

In the final presentation of the session, Heidi Danker-Hopfe (Charité University, Berlin, Germany) expanded on the relation between temperature regulation and sleep. She explained that there is a circadian variation in body temperature and that humans sleep when their core temperature is low and are awake when it is high. Sleep initiation coincides with the decrease in body temperature, while the body awakes when the core temperature rises. The ventrolateral part of the preoptic area in the brain is involved in sleep-wake regulation and contains warm- and cold-sensitive neurons that are also involved in thermoregulation. In older people, the circadian variation in core temperature is less than in younger people, which may have an effect on sleep latency. Behavioral changes such as warming the feet before going to bed may have a positive effect on this. It is still an open question whether changes in sleep electroencephalogram (EEG) observed under RF field exposure result from subtle temperature changes induced by absorbed power or from other effects.

In summary, science has provided a deeper insight into the molecular and physical aspects of heat sensation and heat response regulation. In combination with the knowledge on heating by different RF frequencies, this gives a better background for setting exposure limits.

THERMAL SENSITIVITIES

The primary recognized mechanism for the effect of RF fields on the body is heating, and so it is important

that RF guideline development takes into account the effects that temperature has on the body. Although there is a considerable body of research concerning the effect of RF on thermally-mediated biological effects, it is not as comprehensive as that relating to thermally-mediated effects that are independent of RF. This session draws on knowledge from the latter research domain in order to better understand the consequences of RF-induced temperature change in the body. The presentations in this session covered a range of heat-induced effects, including the body's normal thermoregulatory response, limitations to this thermoregulatory mechanism, and damage to specific tissues and organs.

Eugene Kiyatkin (NIDAIRP, Baltimore, MD) focused his presentation on the brain and importantly noted that it is unusual to think in terms of "thresholds" for thermally induced brain damage (due to the large number of factors that determine such damage). Crucial to this view is that it is absolute temperature and not merely temperature change that determines harm and that absolute temperature is dependent on a number of factors. For example, certain drugs and behaviors can cause brain temperature fluctuations of 2–3 °C, and without knowledge of these factors it is difficult to determine the effect of an additional heat load (such as from RF). It was also noted that environmental heat had very little effect on brain temperature due to the efficiency of the thermoregulatory system and that the main effect on brain temperature was due to challenge, such as from certain drugs (e.g., ± 3,4 methylene-dioxy-methamphetamine inhibiting heat loss via vasoconstriction) and behaviors (e.g., wearing clothing that inhibits heat loss to the environment). This raises an important issue for RF guideline development because the greatest thermal effects relate to factors that are likely to be independent of the RF-generated heat itself.

Andreas Flouris (University of Thessaly, Greece) noted that current occupational guidelines limiting exposure to heat were designed to protect workers from increasing body core temperature beyond 38 and 38.5 °C, for non-acclimatized and acclimatized workers, respectively, and do so by restricting work rates in accordance with different work environments. However, he presented research demonstrating that important thermoregulatory changes can occur (such as increases in metabolic rate) in the absence of changes to body core temperature, and it may not be sufficient in the development of guidelines to treat body core temperature change as the primary endpoint of concern for thermal stress. Flouris also presented research demonstrating that thermoregulatory mechanisms were less efficient in females (relative to males) and in those over approximately 48 y of age (relative to younger adults). Combining this, he recommended that considerations of thermal stress take into account multiple endpoints (such as metabolism, body temperature, perceived strain, and heart rate) and also age and gender.

Pavel Yarmolenko (Washington) provided background on the use of mild hyperthermia for enhancing drug delivery, whereby mild hyperthermia increases blood perfusion around a target site and affects drug delivery via a range of mechanisms (cellular metabolism, stress response, proliferation, and survival). This technique requires considerable knowledge of damage thresholds in order to avoid harm to the patient, with a number of key findings of particular relevance to guideline development. Yarmolenko stressed the diversity in both an organ's ability to thermoregulate and its damage threshold, and that our knowledge of these is limited to a subset of tissue types. Similar to Flouris, he noted that, as a function of duration, absolute temperature over time, rather than energy deposition, is the most relevant metric for predicting damage. Yarmolenko introduced the concept of thermal dose isoeffect, whereby the thermal history of tissues is converted to an equivalent number of minutes of heating at 43 °C. This is expressed as cumulative equivalent min at 43 °C (CEM43). This metric is also a candidate for guidance in medical applications (see Session 4). It was also noted that although this estimate of tissue damage is in principle linear and can be extrapolated to thermonormal conditions, the "linear" nature of the relationship is very much an assumption and has not yet been borne out by research.

Masami Kojima (Kanazawa Medical University, Japan) presented research from his laboratory addressing the mechanisms of ocular damage from millimeter wave (40 GHz, 95 GHz) and infrared-A (808 nm) exposures. Infrared-A, 40 GHz, and 95 GHz exposures resulted in different temperature distributions within the eye, with conduction, wide convection, and intense convection mechanisms responsible for this, respectively. These thermal mechanisms resulted in different damage patterns, with thresholds in the cornea for acute minor damage of 21 to 40 min CEM43, for acute significant damage of 41 to 22,000 min CEM43, and for severe damage above that. Kojima noted that his research also suggests that the 6-min averaging period used by ICNIRP in its guidelines is sufficient for ocular damage evaluation.

Roger Mieusset (CHU Toulouse, France) described the research relating testicular temperature to sperm count, mobility, and morphology, where there is clear evidence that elevated testicular temperature (>35 °C) is detrimental to all three metrics. He described research that has demonstrated that there is substantial variability in testicular temperature (32–36.5 °C), with important determinants of this including posture (2 °C increase due to sitting relative to walking), sleep state (1.2 °C increase during sleep relative to daytime awake), and clothing (1.5–2 °C increase when clothed relative to being naked). Mieusset noted that 35 °C could be taken as a threshold for harm; that the longer the increased temperature, the greater the harm; that a 10 g averaging

mass is consistent with the size of the testes, but that there was no research testing whether temperatures within smaller volumes were better predictors of harm; and importantly, that there is no adaptation to recurrent elevated testicular temperatures.

In summary, the presenters consistently emphasized the complexity of the relationship between temperature and harm, particularly in that it is variable across tissue and organ type. It was also noted that it is possible that physiological temperatures may already cause harm under certain conditions, regardless of whether there is exposure to RF. The presenters were also consistent in emphasising the role of absolute temperature (rather than temperature change) in determining injury. This limits the degree of control over harm that RF guidelines can achieve as they do not have control over pre-exposure temperatures, but only RF-induced temperature change. However, it was clear from the presentations that in itself, RF-induced temperature elevations under normal circumstances are very small relative to the magnitude of normal temperature variability. A difficulty raised within the presentations is that while a great deal of our knowledge of temperature/harm relations is based on the concept of "CEM43 minutes" at mild (or greater) hyperthermia, it is not clear that this concept can be extrapolated down to the temperature range that would be more relevant to RF exposure within ICNIRP guideline values.

THERMAL EFFECTS DUE TO RF EXPOSURE AND RF DOSIMETRY

The thermal effects due to exposure to RF fields were addressed in this session. Computational modeling has improved significantly within the last few years and is often the method of choice to determine temperature as direct measurements are not only costly and complex but are also limited due to ethical reasons, especially for excessive heat. Special attention was given to temperature-sensitive organs and sensitive groups within the population, such as children, pregnant women, and the elderly.

Kenneth Foster (University of Pennsylvania) summarized the established mechanisms for thermal effects. He began with consideration of the Arrhenius equation and the typical 1.5- to 3-fold increase in reaction rate by a 10 °C temperature increase, and progressed to more sensitive systems like the TRP channels. Any change in temperature may result in biological effects and some of the postulated "non-thermal" effects of RF fields (like the induction of heat shock proteins in *C. elegans* or the changes in EEG observed in volunteers) may be attributed to small or subtle increases in temperature.

Short RF pulses (in the μs-range) at high power density (W cm^{-2}) can cause an auditory effect, which is due to a thermoelastic expansion of the tissues in the head. The effect is considered as annoyance. Thermally-induced membrane depolarization can also occur, but only at very high peak SARs (tens of W kg^{-1}), far too high to be relevant in setting guidelines.

The question of how much precision was needed in thermal and spatial averaging was raised. Unfortunately, there is very little new information to add to the Pennes Bioheat Equation from 1948. Compared to convection and radiation, heat transfer through conduction is the most common way of averaging thermal exposure. Foster did not argue for a change in the 6-min averaging period or the 10-g averaging mass currently in use by ICNIRP.

Akimasa Hirata (Nagoya Institute of Technology, Japan) uses computational modeling to simulate temperature changes in the human body due to ambient heat or RF exposure. His work includes electromagnetics and thermodynamics in anatomically-realistic models (which have more than 50 different tissue types). These models also have thermoregulatory responses (vasodilation and sweating) and have been validated by measurements. Modeling of perspiration showed an age dependency as the sweating rate declined in the elderly (starting from around 40 y old). No significant differences in the thermoregulatory responses (to ambient heat) were observed in pregnant women or children.

Also for whole-body averaged SAR, the modeled temperature increase in different human models and at different frequencies correlated nicely with measured temperature changes. At a whole-body SAR of 4 W kg^{-1}, the core temperature in the elderly increased by 0.9 °C at 30 min, which was significantly higher compared to younger adults, due to the lowered sweating rates in the elderly. The core temperature elevation in children was smaller than those in adults due to their higher body surface area to mass ratio. In addition, this work does not support the concept that children have impaired thermoregulatory responses to exercise in the heat.

Taking the human head as an example of localized exposure to RF fields, heat diffusion would smooth the distribution of the temperature increase compared to the SAR distribution. Also it was found that an averaging mass of 8 to 20 g for localized SAR was a good metric to estimate the temperature elevation. The best averaging algorithm for frequencies up to 10 GHz was to average over multiple and contiguous tissues without the pinna.

Due to the poor heat removal capacity of the eye, microwave-induced cataract formation is still a topic of concern. Under whole-body exposures at 2.45 GHz, the core temperature in human and rabbit models reached a 1 °C increase before the critical temperature of 41 °C was reached in the lens. For localized exposures, the temperature elevation at the skin surrounding the human eye

reached the critical temperature of 43 °C before the lens reached a temperature of 41 °C. Hirata concluded that the ICNIRP guidelines are conservative regarding the risk of cataract formation.

Marvin Ziskin (Temple University, Philadelphia, PA) discussed the impact of thermal effects, with dividing cells being the most sensitive to insult by heat. If cells within mature organs are affected, they are replaced, but if cells are affected in the embryo and fetus, cell death becomes a major, non-reversible effect. Hyperthermia is a well-known teratogen in mammals but also in birds. Skeletal malformations, brain defects (such as microcephaly, encephalocoele and exencephaly) and neural tube defects are the best studied fetal abnormalities in rodents and guinea pigs; these occur at less than 1 min CEM43. A continuous temperature elevation of 1.5 °C did not result in developmental abnormalities, but the time of exposure becomes critical with increasing temperature: for a 2 °C increase, exposure times of up to 32 min were observed to be safe; for a 4 °C increase, this time was reduced to 2 min; and at a 6 °C increase, developmental abnormalities were observed after exposure times of less than half a minute. Factors that may help to prevent harm in humans include highly efficient thermoregulation mechanisms as well as enhanced repair mechanisms.

Finally, Ziskin discussed the effects of millimeter (mm)-waves on the skin. Russian and Ukrainian scientists reported successes in mm-wave therapy for many different symptoms and pathologies many decades ago. Similar studies are rare in Western countries and any benefit to health is still under discussion. Ziskin systematically studied the effects of blood perfusion on temperature increase (exposure at 0.2 W cm^{-2} and 42.5 GHz) due to the use of vasodilating creams and blood pressure cuffs. The skin temperature increase was greatly affected by blood flow. The warmth detection threshold depends on the frequency, which is closely correlated with the penetration depth.

Christopher Collins (NYU School of Medicine, NY) introduced the topic of magnetic resonance imaging (MRI) and the different fields one is exposed to during a scan. The heating pattern in MRI depends largely on sample geometry and heterogeneity showing a higher local SAR in heterogeneous objects. Great variations in SAR distribution are observed not only in different positions but also between individuals even with similar builds. In the brain, which is difficult to heat compared to other tissues, absorption was increased with frequency when 200, 300, and 340 MHz were compared. Based on simulation studies with realistic MR pulse sequences, it was concluded that time averaging over several seconds is adequate for determining the temperature increase in MRI. Local blood perfusion has to be considered in computational modeling, as it increases significantly (>10-fold) with temperature even in deep tissues. The local SAR can change in the

order of minutes during a 1-h scan, and thus it is necessary to consider SAR distributions over a longer time scale.

In summary, relevant data for thermal injury are scattered, and knowledge on the boundaries between small thermal effects (without health relevance) and obvious damage are still limited. The data presented did not challenge the present guidelines.

LESSONS LEARNED FROM MEDICAL APPLICATIONS

RF fields are used in many clinics and hospitals throughout the world for imaging, diagnosis, or therapy. Ideally, imaging or diagnosis should not produce any overt biological changes in exposed tissues, whereas therapy must produce appropriate biological responses to be an effective remedy. Therefore, the thresholds of most interest to ICNIRP regarding thermal effects of RF fields are likely to occur somewhere between the exposures used for imaging or diagnosis and those used for therapy. There is a long history of using heat in the treatment of cancer, and experience with hyperthermia should be particularly informative since exposures will occur at levels well above nominal guideline values.

Gerard van Rhoon (Erasmus MC Cancer Institute, the Netherlands) explained that it is difficult to increase the average temperature of patients using the deposition of RF power. Generally, people have a very efficient physiological mechanism to limit temperature increase under thermal stress, such that RF-induced hyperthermia can be safely applied even to frail, elderly people. Localized high temperatures at the skin are sensed as a burning pain, while high temperatures at depth are usually perceived as a pressure pain or urging. Responding to symptoms of pain is usually sufficient to avoid thermal damage (although symptoms usually only develop after 20 min or so of exposure), and while the location of pain can be well correlated with predicted energy hot spots, feelings of pain are largely independent of maximum SAR value. A few instances of nausea and other mild symptoms were sometimes reported in a study with 16 patients following prolonged hyperthermia of the neck and head, but overall exposure did not produce any consistent neurological effects. The local SAR in the brain was calculated to be up to 24 times the ICNIRP basic restrictions for workers. The lack of effects was attributed to the ability of the brain to regulate its temperature by increasing blood perfusion rates.

The role of temperature in cancer immunology was described by Elisabeth Repasky (Roswell Park Cancer Institute). Experimental studies indicate that housing mice at thermoneutral temperature (29–31 °C) can significantly slow tumor growth and reduce metastatic tumor

numbers compared to using standard laboratory temperature (18–24 °C). These responses were mediated by the action of the sympathetic nervous system on the immune system, by increasing numbers of cytotoxic T cells and decreasing myeloid-derived suppressor cells at thermoneutrality. Overall, it was concluded that ambient temperature can have a powerful influence on the anti-tumor immune response, particularly in animals with cancer.

Theodoros Samaras (Aristotle University of Thessaloniki, Greece) described a recently proposed guideline for limiting exposure to RF fields during MRI that is based on the use of CEM43 as a model to calculate thermal dose thresholds (van Rhoon et al. 2013). Using published values of thresholds for thermal damage in different tissues, it was suggested that for all people, the maximum local temperature of any tissue should be limited to 39 °C. Under the supervision of a medical or trained person (controlled conditions) the thermal dose should be less than 2 min CEM43 for the elderly, children and others with impaired (systemic or local) thermoregulation and less than 9 min CEM43 for people with unimpaired thermoregulatory ability. However, further refinements of the proposal may be necessary. For example, this model may not be valid for very low or very high temperatures; the value of the constant, R is still under discussion; and the proposed guideline derives from thresholds of all tissues and not just the peripheral tissues that are most exposed during MRI. Finally, it was stressed that effects of local heating must be considered to avoid thermal damage.

This last point was amplified by Manuel Murbach (IT'IS, Zürich, Switzerland) who examined tissue heating during MRI examinations. With advances in computational dosimetry producing ever more realistic models with which to assess exposure, it is clear that it is possible to be compliant with the limits for whole body SAR in MRI (as specified by IEC 60601-2-33) and so provide sufficient protection against whole-body heating, but to exceed the limits of peak local SAR, particularly in peripheral tissues where significant heating may occur. However, strict compliance with limits on local SAR would be too conservative. An alternative concept for MRI was proposed where limits would be based on thermal dose, not SAR or temperature. This would introduce issues that needed to be clarified, including agreement on the safe thermal dose limit (i.e., 2 min CEM43) and the minimum interval between scans. Particularly exciting were future developments that might allow the modeling of individual thermal responses of patients to be used to maximize imaging quality without the risk of causing harm.

Using models published by the previous speaker, Johan van den Brink (Philips Healthcare, Best, the Netherlands) analyzed the results of 17,100 real-life scans for temperature and thermal dose values. It was found that the peak local temperatures in patients with normal thermoregulation remained below 40 °C and less than 0.5 min CEM43 (when scanned in first level mode as defined by IEC 60601-2-33). However, the temperature could slightly exceed 40 °C in the extremities of patients with impaired thermoregulation, but remained less than 2 min CEM43 even in such patients with a slight fever. Overall, it was concluded that these data corroborated the historical safety experience with MRI and suggested that the existing safety control measures were sufficient.

The effects of RF fields on the temperature rise of implanted medical devices were described by Earl Zastrow (IT'IS, Zürich, Switzerland). Theoretical computations using a simple, elongated wire suggested that people with implants were not sufficiently protected by the existing ICNIRP guidelines from the possibility of highly localized thermal effects, and that an averaging mass of 10 g used in these guidelines was too large to provide a detailed description of the increase in temperature. During maximal MRI imaging of the head of a person with a deep brain stimulator, localized temperatures at the tip of the implant could be increased by up to 100 °C, while thoracic imaging would induce temperature rises of about 20 °C (both cases neglect all effects of thermoregulation, which complicates interpretation). Overall, these data highlighted the need for further risk-benefit considerations for implants in MRI.

In summary, no specific thresholds for damage were identified, but the session provided reassurance that the existing standards and guidelines used to limit exposures of patients to RF fields during MRI generally provide an adequate margin of safety, with temperature increases usually remaining within acceptable boundaries. People usually have highly efficient thermoregulatory mechanisms, such that it can be difficult to increase whole-body temperature using RF power. It was possible to be compliant with limits on whole-body SAR but exceed the limits on local SAR, which could lead to localized heating. The magnitude of any localized heating depends on (the increase in) blood perfusion rates through the exposed tissues. Feelings of pain (in the skin or deeper tissues) can be used as a reliable indicator to avoid tissue damage. It was suggested that formulating standards based on the thermal isoeffect dose (CEM43) may provide a better rationale than using either SAR or temperature. Lastly, further work is required regarding the temperatures that might be induced by the imaging of implanted medical devices.

WORKSHOP ROUNDUP AND CONCLUSION

The final session of the workshop was devoted to a panel discussion that summarized the salient information that had been presented in the previous sessions and formulated conclusions regarding thresholds for thermal damage

that ICNIRP could consider as part of its revision of its RF guidelines. Several questions had been shared with all participants in advance, and the contributions were first requested from the speakers and then from all participants.

The first important conclusion was that there is a large body of evidence showing that, at the level of the whole organism, nothing is unexpected: the knowledge on thermoregulation mechanisms and on temperature sensitivity of biological systems and tissues is such that a consensus can be reached regarding RF exposure as one of many heat sources. A clear distinction was made between the known thresholds for thermal damage and the potential health effects of RF exposure at the low levels related to wireless communications.

Another conclusion was that what matters most in relation to thermal damage (adverse health effects) is the absolute temperature (T) more than temperature elevation (ΔT).

Duration of whole-body RF exposure is a critical parameter that often determines the effect threshold. It was emphasized that acute exposure (minutes) can lead to acute biological effects and further to lasting health effects. This is clearly demonstrated by the use of the CEM43 model to assess thresholds of thermal damage. Consequences of thermal exposure to RF fields also depend on timing (circadian effects) and other ongoing thermoregulation (influenced by external temperature and humidity levels).

The 6-min averaging time that is used for exposure assessment in the present RF guidelines from ICNIRP was discussed briefly. Based on the rationale for selecting this value, it was agreed that this was valid for whole-body exposures but with a large uncertainty. However, this value could be set closer to 30 min for localized exposures, and to less than one minute for implanted medical devices.

Local exposure thresholds are more difficult to determine as exposure conditions of tissues can vary greatly. Organs and tissues need to be able to eliminate heat effectively, but the possibility of RF-induced hotspots complicates this process.

In several presentations, a clear emphasis was placed on the crucial role of the head in terms of thermoregulation (potential difference between head and core temperature).

Effects of local RF exposure mediated by temperature sensors (e.g., TRP receptors) were discussed as examples of the elicitation of biological effects, and possibly health effects (e.g., sleep disturbance) without direct heating of tissues and organs. This was not considered as "thermal damage" per se, as the thermoregulatory system was "fooled" by signals that incorrectly indicated that there was a heat load on the body.

Overall, the information presented at the workshop will provide valuable input into the revision of the guidelines being formulated by ICNIRP for limiting human exposure to RF fields. However, it was clear that some uncertainties remain regarding thermal thresholds, and further information would be beneficial in some areas, particularly regarding variations in temperature sensitivity in individuals who may be at particular risk (in both health and illness) and between different tissue types within the body.

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