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Models for evaluation of thermal hazard in medical diagnostic ultrasonic fields

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ELECTROTECHNICAL
COMMISSION

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INTERNATIONAL ELECTROTECHNICAL COMMISSION

MODELS FOR EVALUATION OF THERMAL HAZARD IN MEDICAL DIAGNOSTIC ULTRASONIC FIELDS

FOREWORD

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IEC 62799, which is a technical report, has been prepared by IEC technical committee 87: Ultrasonics.

The text of this technical report is based on the following documents:

Enquiry draft	Report on voting
87/510/DTR	87/537/RVC

Full information on the voting for the approval of this technical report can be found in the report on voting indicated in the above table.

This publication has been drafted in accordance with the ISO/IEC Directives, Part 2.

Terms appearing in bold print in the text are defined in Clause 3 of this technical report.

The committee has decided that the contents of this publication will remain unchanged until the stability date indicated on the IEC web site under "http://webstore.iec.ch" in the data related to the specific publication. At this date, the publication will be

- reconfirmed,
- withdrawn,
- replaced by a revised edition, or
- amended.

A bilingual version of this publication may be issued at a later date.

MODELS FOR EVALUATION OF THERMAL HAZARD IN MEDICAL DIAGNOSTIC ULTRASONIC FIELDS

1 Scope

This technical report provides background information for users of IEC 62359 to understand the relative merits of several of the potential replacements for the thermal index (TI) as described in IEC 60601-2-37 and IEC 62359.

The report discusses:

– parameters related to thermal aspects of diagnostic ultrasonic fields;
– methods for the determination of an exposure parameter relating to temperature rise in theoretical tissue-equivalent models, resulting from absorption of ultrasound.

The report is intended to be used by:

– those involved in the development and maintenance of IEC 62359;
– manufacturers of medical electrical equipment for risk assessment;
– health care regulatory authorities, test houses and other organizations responsible for implementing standards for medical electrical equipment.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

IEC 60601-2-37:2007, *Medical electrical equipment – Part 2-37: Particular requirements for the basic safety and essential performance of ultrasonic medical diagnostic and monitoring equipment*

IEC 62127-1:2007, *Ultrasonics – Hydrophones – Part 1: Measurement and characterization of medical ultrasonic fields up to 40 MHz*

IEC 62127-2, *Ultrasonics – Hydrophones – Part 2: Calibration for ultrasonic fields up to 40 MHz*

IEC 62359:2010, *Ultrasonics – Field characterization – Test methods for the determination of thermal and mechanical indices related to medical diagnostic ultrasonic fields*

3 Terms and definitions

For the purposes of this technical report, the terms and definitions given in IEC 60601-2-37, IEC 62127-1, IEC 62127-2 and IEC 62359, some of which are repeated below for convenience, and the following terms and definitions apply.

3.1
acoustic absorption coefficient
μ
quantity intended to account for loss of ultrasonic energy to tissue at a specified point by mechanisms other than scattering

Note 1 to entry: **Acoustic absorption coefficient** is expressed in nepers per centimetre (Np cm^{-1}).

Note 2 to entry: The **acoustic absorption coefficient** must be less than or equal to the **acoustic attenuation coefficient**.

3.2
acoustic attenuation coefficient
α
quantity intended to account for reduction of energy of an acoustic wave by all mechanisms involving interaction of the wave and all matter between the source and a specified point

Note 1 to entry: **Acoustic attenuation coefficient** is expressed in nepers per centimetre (Np cm^{-1}).

Note 2 to entry: The **acoustic attenuation coefficient** must be greater than or equal to the **acoustic absorption coefficient**.

Note 3 to entry: The **acoustic attenuation coefficient** does not account for geometric attenuation.

3.3
acoustic working frequency
f_{awf}
frequency of an acoustic signal based on the observation of the output of a hydrophone placed in an acoustic field at the position corresponding to the spatial-peak temporal-peak acoustic pressure

Note 1 to entry: The signal is analysed using either the **zero-crossing acoustic-working frequency** technique or a spectrum analysis technique. Acoustic working frequencies are defined in 3.3.1 and 3.3.2.

Note 2 to entry: In a number of cases the present definition is not very helpful or convenient, especially for broadband transducers. In that case a full description of the frequency spectrum should be given in order to enable any frequency-dependent correction to the signal.

Note 3 to entry: **Acoustic working frequency** is expressed in hertz (Hz).

SOURCE: IEC 62127-1:2007, 3.3.

3.3.1
zero-crossing acoustic working frequency
number, n, of consecutive half-cycles (irrespective of polarity) divided by twice the time between the commencement of the first half-cycle and the end of the n-th half-cycle

Note 1 to entry: Any half-cycle in which the waveform shows evidence of phase change shall not be counted.

Note 2 to entry: The measurement should be performed at terminals in the receiver that are as close as possible to the receiving transducer (hydrophone) and, in all cases, before rectification.

Note 3 to entry: This frequency is determined according to the procedure specified in IEC/TR 60854.

Note 4 to entry: This frequency is intended for continuous wave systems only.

3.3.2
arithmetic-mean acoustic working frequency
arithmetic mean of the most widely separated frequencies f_1 and f_2, within the range of three times f_1, at which the magnitude of the acoustic pressure spectrum is 3 dB below the peak magnitude

Note 1 to entry: This frequency is intended for pulse-wave systems only.

Note 2 to entry: It is assumed that $f_1 < f_2$.

Note 3 to entry: If f_2 is not found within the range $< 3 f_1$, f_2 is to be understood as the lowest frequency above this range at which the spectrum magnitude is -3dB from the peak magnitude.

3.4
non-scanning mode
mode of operation of a system that involves a sequence of ultrasonic pulses which give rise to ultrasonic scan lines that follow the same acoustic path

SOURCE: IEC 62127-1:2007, 3.39.4.

3.5
peak-rarefactional acoustic pressure
p_-; p_r
maximum of the modulus of the negative instantaneous acoustic pressure in an acoustic field or in a specified plane during an acoustic repetition period

Note 1 to entry: **Peak-rarefactional acoustic pressure** is expressed as a positive value.

Note 2 to entry: **Peak-rarefactional acoustic pressure** is expressed in pascal (Pa).

Note 3 to entry: The definition of **peak-rarefactional acoustic pressure** also applies to peak-negative acoustic pressure, which is also in use in literature.

SOURCE: IEC 62127-1:12007, 3.44.

3.6
safe use time
SUT
maximum duration of exposure in a region at a particular output level that would be no more hazardous than scanning at a specified **threshold exposure**

Note 1 to entry: **Safe use time** is expressed in seconds (s).

3.7
scanning mode
mode of operation of a system that involves a sequence of ultrasonic pulses which give rise to ultrasonic scan lines that do not follow the same acoustic path

Note 1 to entry: The sequence of pulses is not necessarily made up of identical pulses. For instance, the use of sequential multiple focal-zones is considered a scanning mode.

SOURCE: IEC 62127-1:2007, 3.39.5.

3.8
temperature rise
ΔT
difference between the instantaneous temperature and the normal physiological temperature of the subject

Note 1 to entry: **Temperature rise** is expressed in degrees Celsius (°C).

Note 2 to entry: **Temperature rise** may be either positive or negative.

3.9
thermally equivalent time
t_{43}
at a constant temperature of 43 °C, duration of exposure required to produce the same magnitude of a thermally induced bio-effect, i.e., an "iso-effect", as is produced by an exposure of duration t' at a different temperature T that may vary in time

The thermally equivalent time (t_{43}) is defined mathematically as:

$$t_{43} = \int_0^{t'} R^{\,[T(t)-43°C]/C_T}\, dt$$

where:

C_T = 1 °C, a constant to render the exponent dimensionless;

$T(t)$= temperature (which may vary in time) producing the bioeffect;

t = time;

t' = time required to produce the bioeffect at temperature T;

R = thermal normalization constant, equal to 4,0 if $T \leq 43$ °C;

R = thermal normalization constant, equal to 2,0 if $T > 43$ °C

Note 1 to entry: In the scientific and medical literature, **thermally equivalent time** is commonly called “thermal dose”.

Note 2 to entry: The general expression for **thermally equivalent time** is $t_1/t_2 = R^{(T_2-T_1)/1°C}$, where R is the thermal normalization constant. Because R varies with both temperature and species, as well as among different tissues within the same species, it must be determined empirically. For simplicity, the values for R are usually fixed at $R = 2$ for $T > 43$ °C and $R = 4$ for $T \leq 43$ °C. More generally, $T1$ is a constant reference temperature, and $T2$ is a function of time.

Note 3 to entry: When quantifying exposure to most forms of radiation, the general term 'dose' is usually expressed in units of absorbed energy (in joules) or specific energy (e.g., J/ kg) rather than in units of time. Although there is a growing preference within IEC to use the more precise term ‘**thermally equivalent time**’, this new term has not yet been carefully evaluated or widely accepted.

Note 4 to entry: The SI unit of **thermally equivalent time** is second (s).

3.10
thermally equivalent time displayed
TETD
exposure duration required to obtain a **thermally equivalent time** sufficient to induce harm in a specified fraction of exposed subjects at a specified point as estimated using a specified model

Note 1 to entry: **Thermally equivalent time displayed** is expressed in seconds (s).

3.11
thermally equivalent time index
thermal dose index
TETI
ratio of the **thermally equivalent time** calculated assuming that $T(t) = (TI + 37) \times 1$ °C and $R = 4$ to a **thermally equivalent time** below which the risk of an adverse thermal effect is very low.

The simplest form of the thermally equivalent time index ($TETI$) is given by the following expression:

$$TETI = \frac{(4)^{TI} \cdot t}{N},$$

where:

TI = **thermal index;**

t = exposure duration;

N = a normalizing factor

Note 1 to entry: The normalizing factor is the **thermally equivalent time** below which the risk of an adverse thermal effect is very low.

Note 2 to entry: **Thermally equivalent time index** is non-dimensional.

3.12
thermal index
TI
ratio of attenuated acoustic power at a specified point to the attenuated acoustic power required to raise the temperature at that point in a specific model by 1 °C

SOURCE: IEC 62359, 3.56.

3.13
thermal load
TL
Thermally equivalent time calculated assuming a constant temperature equal to the value estimated at the **safe use time**, a duration equal to the **safe use time**, R = 4, minus the **safe use time**

Note 1 to entry: **Thermal load** is expressed in seconds (s).

3.14
threshold exposure
exposure to ultrasound which produces a specified constant **temperature rise**, ΔT, that is maintained for a specified duration, t

Note 1 to entry: A **threshold exposure** has a **thermally equivalent time**. For example, if a subject having a normal physiologic temperature of 37 °C experiences an increase in temperature to 41 °C for 4 min, then ΔT = 4 °C and dt = 4 min, and the **thermally equivalent time** is 4 min × 4^4 = 1 024 min = 61 440 s.

3.15
threshold temperature rise
ΔT_{thr}
minimum temperature increase above normal physiologic level required to induce harm in the exposed tissue

Note 1 to entry: **Threshold temperature rise** is expressed in degrees Celsius (°C).

3.16
time to threshold
TT
exposure duration required to raise the temperature at a specified point by the **threshold temperature rise**

Note 1 to entry: **Time to threshold** is expressed in seconds (s).

4 Background

4.1 General

The safety of diagnostic ultrasound is currently assessed and communicated to the user under international standards IEC 62359 and IEC 60601-2-37, respectively. Although originally adopted in 2005 and 2003, these standards are based on work first published in 1992 as the so-called Output Display Standard (ODS), a joint effort of the American Institute of Ultrasound in Medicine and the (US) National Electrical Manufacturers Association [1][1)]. Much has been learned in the intervening fifteen years, and several reviews of the relevant literature, both general [2]-[4] and specific [5], [6] have appeared since that time. Therefore it is considered prudent to report on such aspects of this information as relate directly to IEC 60601-2-37.

1) Numbers in square brackets refer to the Bibliography.

It is well known that there are two broad categories of mechanisms whereby ultrasound may adversely affect biological material, nonthermal (or mechanical) and thermal. As it passes through tissue, diagnostic ultrasound necessarily induces a mechanical strain. This strain is highest in proximity to gas or vapour bubbles, and therefore mechanical damage is most likely to be induced where they are located. Ultrasound is also absorbed as it propagates, and the absorbed energy produces an increase in temperature of the tissue. Depending on the magnitude and duration of the increase, thermal damage to the tissue (or organism) may result. The goal of this report is to examine various means of quantifying the potential for tissue heating to damage biological tissue, and to suggest approaches for enhancing the safety of diagnostic ultrasound.

4.2 Limitations of the existing standard

International standard IEC 62359 quantifies the likelihood that any tissue heating produced by diagnostic ultrasound will harm a patient by requiring the calculation of a quantity called the **thermal index** (TI) and the display of this calculated value on the video screen of the equipment console. The calculation is based on one of several simplified thermal models described in the standard. The models currently defined include those for soft tissue (TIS), bone at the focus (TIB) and bone near the tissue surface, as for cranial bone, hence (TIC), as well as encompassing both **scanning** and **non-scanning** imaging **modes** [7]. The calculated value will depend on factors such as transmitted energy, imaging mode, beam shape, focal depth, waveform and duty factor, but rather than displaying a specific physical parameter, the TI indicates combinations of output settings that are more likely than others to produce an adverse thermal effect [8].

The general form of the TI is simply the ratio of the instantaneous value of a power parameter defined by the standard to the value of the same parameter required to produce a steady-state temperature rise of 1 °C in the exposed tissue. Although it is tempting to consider the value of the TI to be the actual *in situ* temperature rise, this is not the case. Because the models underlying the TI were made sufficiently simple to be implemented in real time with the limited computational power available in 1992, the TI provides only a relative indication of the maximum possible temperature rise at a specific point along the axis of the acoustic beam. Thus values of the TI obtained for different imaging consoles, or even with different transducers used with the same console, cannot be compared.

Several additional inaccuracies or limitations of the TI have been identified. Some of these were known or suspected at the time the ODS was developed [1], although their full significance was not always completely appreciated. A number of factors directly affecting the computational and display algorithms for the TI are discussed in the following subclauses. Other factors, those primarily affecting the measurement of the physical quantities required for specific calculations, are not addressed in this report.

4.2.1 Linear display

As currently defined, the TI displayed onscreen is linearly proportional to the absorbed power or equivalently, to the *in situ* intensity or temperature. In contrast, the **thermally equivalent time** (also ‘thermal dose’, see Note 1 to entry of 3.9), a well known empirical relationship between the temperature T of a biological system and the time t needed for that temperature to induce a deleterious effect, has an exponential form. Specifically, for any two temperatures, T_1 and T_2, and the corresponding exposure times t_1 and t_2, required to produce the same level of effect, this general relation holds: $t_1/t_2 = R^{(T_2-T_1)/1°C}$, where R is the thermal normalization constant. Hence, it is experimentally determined that the rate of induction, or risk, of a thermal effect increases exponentially with temperature. There is thus a fundamental discrepancy between the displayed value of the TI and its stated goal of quantifying thermal risk from exposure to diagnostic ultrasound. A potential solution to this problem is suggested in 4.1.

4.2.2 Equilibrium temperature

As currently defined, the *TI*-value displayed onscreen is based on the steady-state temperature rise calculated for very long duration exposures from a stationary transducer. There are two difficulties here. First, the time needed to reach the steady state depends strongly on exposure parameters, e.g., the width of the acoustic beam, as well as various physiological factors, e.g., the perfusion rate. Clinical users are generally ignorant of the acoustic field they are using and can only guess at the relevant physiology. Second, in most clinical situations the transducer is moved frequently, and a particular imaging mode may be used for only a few tens of seconds before a different mode is selected. The AIUM suggests considering such motion as an additional safety margin protecting the patient [9], with the size of the margin depending on the time needed to reach the steady-state temperature rise. Most clinical users will not be able to estimate the magnitude of the safety margin, and in fact may not even be aware of its existence. Potential solutions to this problem are suggested in 5.3 and 5.4.

4.2.3 Tissue parameters

The choice of the tissue **acoustic attenuation** and **absorption coefficients** are critical to accurate modelling of the expected tissue temperature rise. The amount of heat deposited is proportional to the product of the local time-average intensity and the absorption coefficient, and the local intensity decreases exponentially with the product of the attenuation coefficient and the distance from the source transducer. As currently implemented, the algorithms for the *TI* assume homogeneous tissue with the slopes of both coefficients equal to 0,3 dB cm^{-1} MHz^{-1}. Of course, real tissues are not homogeneous and usually have higher values for both their **acoustic attenuation** and **absorption coefficients** [10]. This model, homogeneous tissue model H.3, was chosen as a reasonable worst case with regard to patient safety because it tends to overestimate **temperature rise** in most cases. However, by artificially limiting transducer output, this combination of factors may reduce the clinical utility of diagnostic ultrasound in many cases, particularly those involving hard-to-image patients.

4.2.4 Transducer self-heating

Because the transducer elements comprising an imaging probe are not 100% efficient at converting electrical to acoustic energy, heat is produced within the transducer itself. Whenever the energized probe is in contact with the patient, a portion of this heat will be conducted into the adjacent tissues. As currently implemented, the *TI* considers only heating produced by absorption of the acoustic beam, i.e., it does not include a correction for transducer self-heating. This seems reasonable for transcutaneous applications because the temperature rise due to surface heating will be small except within a depth of tissue on the order of the perfusion length, 3 mm to 5 mm [2]. For some intra-cavity applications, and especially in the presence of bone, however, the perfusion length may be significantly larger, and transducer self-heating may heat deeper tissues [11] – [13]. At present, the problem is dealt with by restricting the maximum measured surface temperature of the transducer to a level considered safe for patient contact, 43 °C (IEC 60601-2-37).

4.2.5 Safety limits

As currently implemented, no limit is placed on the value of the *TI* that may be employed in diagnostic imaging. This may be reasonable given the nature of the computational algorithms and the fact that almost any reasonably attainable temperature elevation can be sustained without harm if the duration is short enough, but it leaves the clinical user without guidance as to what should be considered “reasonable”. The options suggested in 5.3 and 5.4 automatically incorporate a solution to this problem.

5 Options for improvement of the existing standard

5.1 General

Potential solutions to at least some of the limitations of the TI discussed above are available in the literature. For example, the nonlinear relation between temperature elevation and potential risk was pointed out in [14], which suggested replacing the current linear display with an exponential display based on the form of the **thermally equivalent time**. The fact that the risk of a thermally induced adverse effect depends on both the magnitude and duration of the increase in temperature was considered in [15], which proposed an improvement to the TI, the **thermally equivalent time index** ($TETI$), to account for both factors. The reliance of the TI on equilibrium temperature rise has been investigated in greater detail [8]. It was proposed to replace the current TI with a new parameter called the **time to threshold** (TT), which displays the estimated duration of imaging required for the **temperature rise** to reach the **threshold temperature rise** for an adverse biological effect. A similar approach was investigated in [16], which proposed a different parameter, the **safe use time** (SUT), to compare a simplified estimate of the **thermally equivalent time** to a threshold for an adverse effect in terms of **thermally equivalent time** rather than temperature rise. These four options are discussed first, followed by a fifth that has not yet been published.

A note on nomenclature: In this document, the widely accepted term “thermal dose” is replaced by the more descriptive term “**thermally equivalent time**”, except when referring to the published literature. The definition of “**thermally equivalent time**” is also more precise in that the reference temperature is fixed at 43 °C.

5.2 Exponential display of the current *TI*

5.2.1 Theory

It is well known that there is a relationship between an elevation above normal physiological temperature and the time needed to induce a deleterious effect in a biological system [2], [3], [17], [18]. Simply put, the higher the temperature rise, the shorter the time needed to produce the effect. For any two exposures at two different temperatures, the ratio of the minimum time t_1 required for the lower temperature T_1 to produce an effect, to the time t_2 required for the higher temperature T_2 to produce the same effect increased by a constant multiple for each degree of temperature difference [19], [20]. For example, if the temperature difference $T_2 - T_1$ = 1 °C, then $t_1/t_2 = R$, while if $T_2 - T_1$ = 2 °C, then $t_1/t_2 = R^2$, etc., where R is the thermal normalization constant. In general, $t_1/t_2 = R^{(T_2-T_1)/1°C}$, and the time calculated using this approach to quantify thermal exposures is termed the **thermally equivalent time**. Empirical values of R vary among species, tissues and biological endpoints. They are also temperature-dependent, with $R \approx 2$ for $T > 43$ °C, increasing by a factor of 2 to 3 for $T < 43$ °C. For simplicity, the values for R are usually fixed at R = 2 for $T > 43$ °C and R = 4 for $T < 43$ °C [20], [21].

The equation for **thermally equivalent time** is based on a thermodynamic or “Arrhenius-type” analysis that has been empirically validated for a number of biological endpoints [20], [22]. The underlying principle is that the thermal damage to a biological system, Ω, which occurs regardless of the temperature of the system, may be modelled as a first-order chemical rate equation. From the Eyring equation for reaction rates in condensed or mixed-phase materials [23], [24], it is possible to show that [25]:

$$\frac{d\Omega}{dt} = k = A \exp\left[\frac{-E_a}{R_g T(t)}\right] \tag{1}$$

where A is an arbitrary constant proportional to the change in entropy, E_a is the activation energy for the damage process, R_g is the gas constant, and T is the absolute temperature (i.e., temperature in units of kelvin) at time t. Equation (1) assumes that the rate, k, at which

damage is produced in a biological system can be characterized by a single activation energy, although this may be an oversimplification. It is further assumed that when the probability of occurrence of an adverse event, i.e., the incidence rate, IR, for the event is small, IR is proportional to the amount of damage that accumulates over the duration of heating t_h. Thus:

$$IR = C\int_0^{t_h} \exp\left[\frac{-E_a}{R_g T(t)}\right] dt \tag{2}$$

where C is a constant with units of t^{-1} and t_h is the duration of heating.

For a **temperature rise** $\Delta T(t)$ above the normal physiologic temperature T_o, the incidence rate for an adverse event relative to the background rate for the same event IR_b, is given by:

$$\frac{IR_1}{IR_b} = \frac{\int_0^{t_h} \exp\left\{\frac{E_a}{R_g[T_o + \Delta T(t)]}\right\} dt}{\int_0^{t_h} \exp\left(\frac{-E_a}{R_g T_o}\right) dt} = \frac{1}{t_h}\int_0^{t_h} \exp\left\{\frac{E_a \Delta T(t)}{R_g T_o[T_o + \Delta T(t)]}\right\} dt \ . \tag{3}$$

The relative increase in the incidence rate above the normal background rate, ΔIR_1, due to the **temperature rise** ΔT, is given by:

$$\frac{\Delta IR_1}{IR_b} = \frac{IR_1}{IR_b} - \frac{IR_b}{IR_b} = \frac{1}{t_h}\int_0^{t_h} \exp\left\{\frac{E_a \Delta T(t)}{R_g T_o[T_o + \Delta T(t)]}\right\} dt - 1 \ . \tag{4}$$

For two different **temperature rises**, ΔT_1 and ΔT_2, both functions of time, there will be two different increases. Since $\Delta T(t)/[1 + \Delta T(t)/T_o] \approx \Delta T(t)$, the ratio of the corresponding increases in rates ΔIR_1 and ΔIR_2, is:

$$\frac{\Delta IR_2}{\Delta IR_1} \approx \frac{\frac{1}{t_h}\int_0^{t_h}\left[\exp\left(\frac{E_a C_T}{R_g T_o^2}\right)\right]^{\Delta T_2 / C_T} dt - 1}{\frac{1}{t_h}\int_0^{t_h}\left[\exp\left(\frac{E_a C_T}{R_g T_o^2}\right)\right]^{\Delta T_1 / C_T} dt - 1} = \frac{\frac{1}{t_h}\int_0^{t_h} R^{\Delta T_2 / C_T} dt - 1}{\frac{1}{t_h}\int_0^{t_h} R^{\Delta T_1 / C_T} dt - 1}, \tag{5}$$

where the constant C_T = 1 °C and the thermal normalization constant $R = \exp\left[E_a C_T / \left(R_g T_o^2\right)\right]$. If ΔT_1 and ΔT_2 are constant and we let $\Delta T_2 = n\Delta T_1$, then:

$$\frac{\Delta IR_2}{\Delta IR_1} = \frac{R^{n\Delta T_1 / C_T} - 1}{R^{\Delta T_1 / C_T} - 1} \ . \tag{6}$$

Equation (6) provides a simple expression for the *relative* change in the rate of induction of an effect due to a **temperature rise** ΔT_2 different from an arbitrarily chosen increase ΔT_1.

5.2.2 Illustrative results for the new thermal index display

Notice that in the numerator of Equation (6), the exponent is a linear function of ΔT_1. As currently defined, the TI is the ratio of the output power (or estimated intensity *in situ*) for a particular machine setting to the power (or intensity) required to produce an estimated **temperature rise** of 1 °C, i.e., TI is a linear function of the output power (or intensity). By keeping the reference **temperature rise** as 1 °C, i.e., by setting ΔT_1 = 1 °C, and using the current definition of TI_{cur} as the relative temperature rise, i.e., $n = TI_{\text{cur}}$, a new definition for the thermal index is obtained:

$$TI_{\text{new}} = \frac{\Delta IR_2}{\Delta IR_1} = \frac{R^{TI_{\text{cur}}} - 1}{R - 1} \ . \tag{7}$$

The new index TI_{new} gives the ratio A/B, where A is an estimate of the maximum rate at which damage is produced by an application of diagnostic ultrasound and B is the estimated damage rate produced by imposing a **temperature rise** of 1 °C. This modification provides an easily understood display that more accurately quantifies the thermal risk from exposure to diagnostic ultrasound.

A comparison of TI_{new} vs TI_{cur} is shown in Figure 1 for R = 4. Notice that the curves intersect at the reference level, i.e., at ΔT_1 = 1 °C and TI_{cur} = 1. When the **temperature rise** is greater than the reference level, i.e., when $\Delta T_2 > 1$ °C, $TI_{\text{new}} > TI_{\text{cur}}$. As TI_{cur} increases, the difference between the two increases exponentially, as is consistent with experimental determinations of the temperature dependence of thermal events.

An expanded view of the low-TI_{cur} region of Figure 1 is shown in Figure 2. For values of TI_{cur} below 1, $TI_{\text{new}} < TI_{\text{cur}}$, indicating that the risk associated with such low-level exposures is less than implied by the current onscreen display of TI. At TI_{cur} = 0, TI_{new} = 0, indicating that when the **temperature rise** is 0, there is no excess risk.

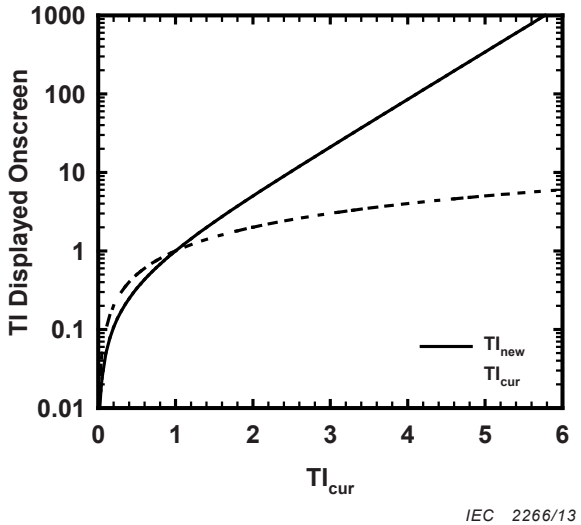


Figure 1 – Comparison of the values of thermal index that would be displayed under the proposed definition, TI_{new}, with that displayed currently, TI_{cur}

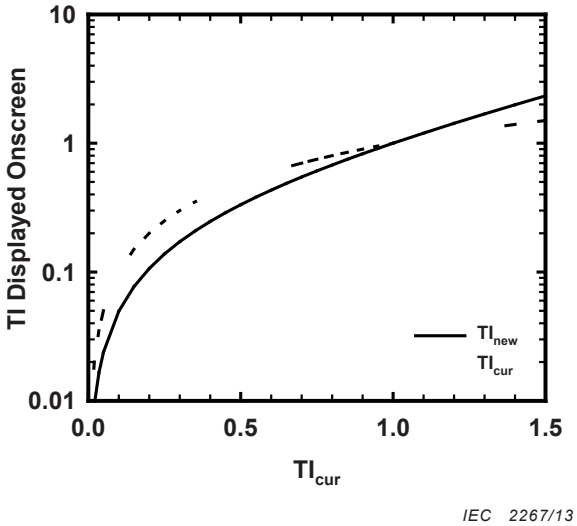


Figure 2 –Expanded view of the comparison of Figure 1 for smaller values of TI_{cur}

5.2.3 Advantages of the new display

The proposed modification to the definition of the TI retains all of the previous work underlying the current **thermal index** plus any improvements to the temperature-estimation algorithms while offering several significant advantages:

- The temperature-dependence of TI_{new} is equivalent to that of the **thermally equivalent time**, which has been verified by numerous experimental results at all levels of biological organization from individual cells to tissues to whole organisms [19]-[22], [26], [27].
- The value displayed onscreen would be a true index of the probability of a thermally induced adverse event. That is, TI_{new} incorporates the concept of the rate of induction of an adverse event relative to an arbitrary reference. The reference chosen corresponds to that of the current TI, although the numerical value of the reference is not known.
- Significantly, TI_{new} = 1 when TI_{cur} = 1. This provides a convenient reference point in the display for sonographers to use when transitioning from the current index to TI_{new}.
- The displayed value could be used to guide the user of a diagnostic scanner in the maximum duration of “safe” imaging of a given region of interest at a particular output level because the form of the expression for TI_{new} is similar to the expression for the **thermally equivalent time**. In this case, “safe” is used in a relative rather than an absolute sense, and the term is interpreted as meaning “no more hazardous than” imaging at the reference output level, $TI_{new} = TI_{cur} = 1$, for a particular time t_1. In other words, if the user images at TI_{new} = 1 for a time t_1, then imaging at a different output, e.g., $TI_{new} = X$, for a time t_1/X would present no greater risk to the patient than the original imaging session.
- The displayed value of TI_{new} may sometimes become quite high. It is hoped this will suggest to users of diagnostic ultrasound machines that examinations are not generally completely free from risk of harm to the patient, and especially that high output levels should be avoided when possible.
- The standard governing the display of the safety indices, IEC 60601-2-37, is currently under maintenance. Therefore, it may be possible to incorporate this proposal into the revised document relatively quickly.

5.2.4 Shortcomings of the new display

The proposed modification to the definition of the TI is subject to some of the same limitations as the current version:

- Nonlinear propagation may occur when the acoustic path contains a significant amount of fluid or other low-attenuation material. The effect increases with output, and because TI_{cur} assumes linear propagation, this can introduce significant error into the calculation for intensity [3]. Technical specification IEC 61949 provides a method for minimizing these finite-amplitude effects when they occur during the calibration procedures for diagnostic transducers and suggests a method for estimating *in situ* exposure. However, use of this method is not currently required when making measurements of the physical quantities needed to determine the TI-value.
- Because TI_{new} incorporates TI_{cur}, it is based on the steady-state **temperature rise** calculated for long-duration exposures from a stationary transducer.
- Because TI_{new} incorporates TI_{cur}, it provides an estimate of risk at a location that may or may not coincide with the region of interest, an effect that may be of particular concern when the foetus is involved.
- It is well known that different **thermally equivalent times** are required for induction of different adverse events [21]. As is the case for the current version of the TI, TI_{new} lacks the ability to quantify risk in absolute terms. This is perhaps its most significant failure.

5.3 Replacement of the TI with the thermally equivalent time index ($TETI$)

5.3.1 Theory

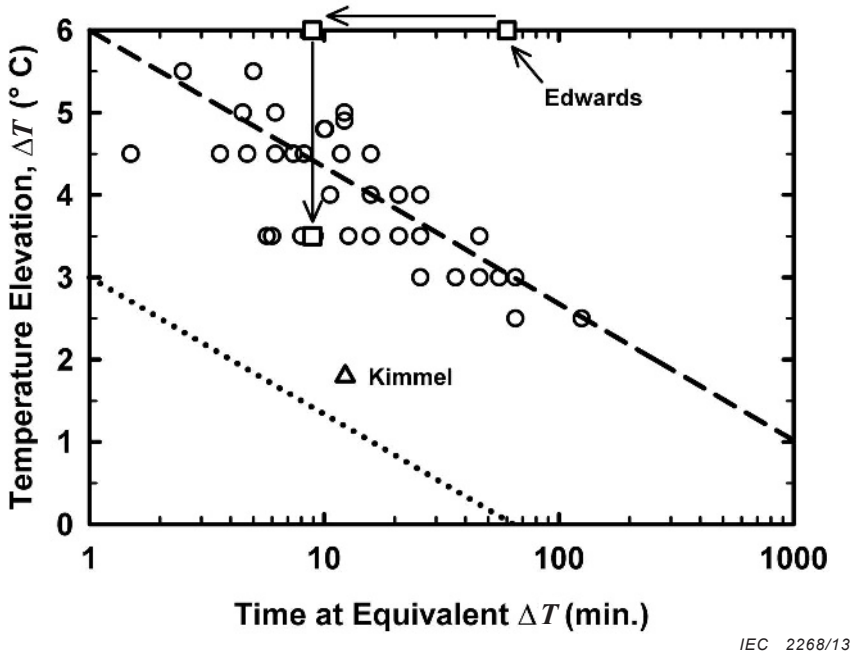
The **thermally equivalent time index** is based on the form of the **thermally equivalent time** but with several simplifying assumptions [15]. To better understand the nature and importance of each of these, the simplest form of the proposed index is given here:

$$TETI = \frac{(4)^{TI} \cdot t}{N}, \quad (8)$$

where TI is the thermal index, t is the exposure duration and N is a normalizing factor equal to a **thermally equivalent time** below which the risk of an adverse thermal effect is very low. By making this choice, exposures in which the $TETI$ is 1 or less will pose very little, if any, risk to the patient of an adverse effect due to a thermal mechanism.

As mentioned in 5.2.1 above, the value of R is assumed to be 2 for $T > 43$ °C, and 4 for $T < 43$ °C. For the first simplifying assumption, the latter value is chosen for the **thermally equivalent time index**. Since the maximum temperature of exposed tissue will rarely, if ever, rise above 43 °C during a diagnostic examination, this is not a significant problem. Second, it is assumed that the maximum **temperature rise** is equal to TI-value. Because the TI-value is the result of a calculation based on anatomic models that incorporate average values for tissue properties, when expressed in degrees Celsius it may differ considerably from the actual *in vivo* **temperature rise**. However, it provides a convenient estimate of temperature elevation to use in the computation of the $TETI$. Third, it is assumed implicitly that the **temperature rise** estimated using the TI-value is relative to the normal, human physiological temperature. Because a common indication for foetal scanning is maternal fever, this assumption is not always valid. However, in order to accommodate the difficulties inherent in the second and third assumptions, a large safety factor is incorporated in the value of N as explained below. Finally, it is assumed that the **temperature rise** estimated using the TI-value is achieved immediately when the exposure begins. Since the tissue temperature takes some time to reach its final value, the assumption represents a small, additional safety factor for the patient.

The value of the parameter N can be selected to suit the subject being examined. For example, the relationship between the temperature and time for producing a foetal malformation was shown to be related to the product of time and the number 4 raised to the magnitude of the temperature elevation [18]. When data obtained from different species are transformed into their thermal equivalents by normalizing them to a common denominator, each organism's normal physiological temperature, the results may be compared and used to determine a safe exposure level [28]. The result of normalization is shown in Figure 3. Each datum was derived from an analysis of a heating-cooling profile of a pregnant laboratory animal (rat, mouse, or guinea pig) which yielded foetuses with teratologic anomalies [22]. The original "safe" boundary line shown in [18], *i.e.*, t_{43} = 1 min, is now given by $t_{43\ -\ 37} = t_6$ = 1 min, shown by the dashed line. About half of the data points in Figure 3 are below this line, indicating that temperature exposures previously considered safe because they fell below the boundary in [18], *i.e.*, below t_{43} = 1 min, are actually potentially harmful. A new "safe" boundary might be drawn at t_4 = 1 min if it were not for a single point [26]. While those data include seemingly minor anomalies and also those with high natural background rates, prudence suggests that the "safe" line be drawn at t_3 = 1 min in Figure 3, as shown by the dotted line. Inserting these values into Equation (8) gives the desired value of N for foetal exposures:

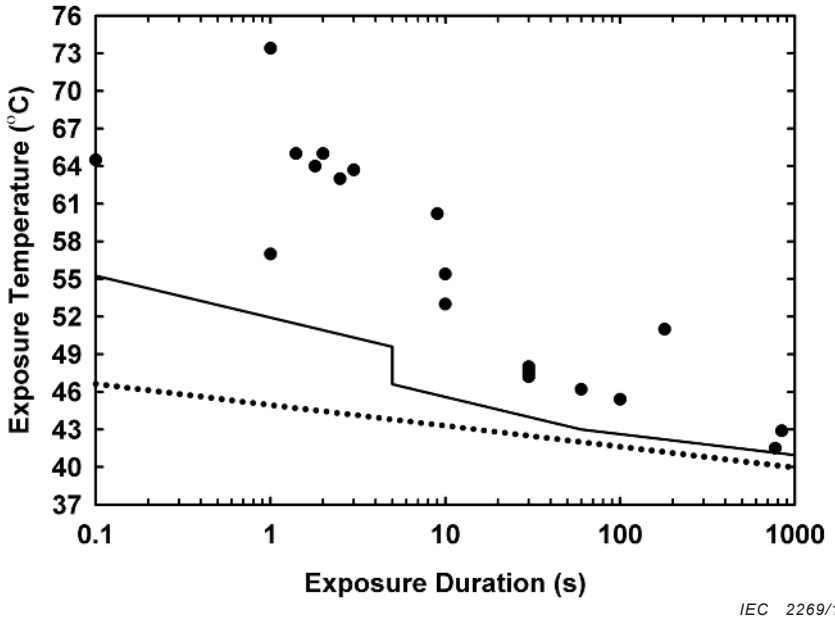


The dashed line is the equivalent lower boundary (t_{43} = 1 min) as determined by [18], and the dotted line is the lower boundary for the 'transformed' data. The open triangle shows the lowest positive-result datum [26], ΔT = 1,8 °C. The open squares and arrows show the 'movement' of a data point from Edwards [29, 30] from its original location in [18] at (60 min, 6 °C) based on maternal exposure time and temperature to its "final" location in [22] at (8,9 min, 3,5 °C) based on thermally equivalent exposures of the foetus. Adapted from [28].

Figure 3 – Thermal-equivalent core temperature elevations *vs* time

$$N = (4)^{TI} \cdot t = (4)^3 \cdot 1\ \text{min} = 64\ \text{min}\ . \tag{9}$$

The case for non-foetal tissues has been investigated [6], resulting in a compilation of threshold-based data that were reported for single-burst ultrasound-exposure durations as short as 100 ms. The data suggested that for non-foetal soft tissue and for scanning conditions consistent with conventional B-mode ultrasound examinations for which the exposure durations at the same *in situ* locations would be less than a few seconds, the allowable maximum temperature increase, ΔT, could be relaxed relative to values represented by the conservative boundary line for longer exposures of non-foetal tissue. The data and the solid line in Figure 4 give the results of the analysis.



The dotted line is the simplified lower boundary (t_{42} = 1 min) suggested for the determination of N in Equation (8) for non-foetal tissues. Adapted from [6].

Figure 4 – Temperature-time curve (solid line) that represents a conservative boundary for non-foetal exposure durations, particularly for exposure durations of less than 5 s

The solid line in Figure 4 has four separate components and a discontinuity at 5 s. The portion of the line on the right-hand side (extending from 60 s to 1 000 s) is the **thermally equivalent time** line for t_{43} = 1 min. This part of the curve lies relatively close to the lowest data point in the figure. Therefore, it is suggested that a lower value, t_{42} = 1 min, be used to calculate the value for N. For simplicity, it is also suggested that the right-hand portion of the curve be extended to the left and used for all exposure durations. In this case, the value of N for non-foetal exposures becomes:

$$N = (4)^{TI} \cdot t = (4)^5 \cdot 1 \text{ min} = 1024 \text{ min} \ . \tag{10}$$

Although this number may seem much too large, it is actually consistent with not only the data shown in Figure 4, which were generated using ultrasound-exposure systems, but also with data from systems using hot water or hot air, radiant heat, etc. Representative data of that type are given in Table 1. Notice that even the most sensitive tissue shown, kidney, would require that the $TETI$ reach a value of 80 before significant damage occurred.

Table 1 – Thermally equivalent time thresholds for chronic damage in various tissues, t_{43}; see [21].

Tissue	**Species**	**Time** (min)	**Lesion**
Muscle and fat	Pig	240	Necrosis, fibrosis
Skin	Man, rat, mouse	210	Epidermal necrosis
Skin	Man, rat, mouse	120	Epilation
Esophagus	Pig	120	Fibrosis
Cartilage	Rat, mouse	120	Necrosis
Bladder	Dog, rabbit	80	Mucosal necrosis
Small Intestine	Rat, mouse	40	Crypt loss
Colon	Pig, rabbit	30	Fibrosis
Liver	Dog	30	Hepatocyte loss, necrosis
Brain	Cat, dog	25	Neural pyknosis
Kidney	Mouse	20	Necrosis of glomeruli and tubules

In the event that the TI varies during an examination, which is certainly not uncommon, the $TETI$ may be more generally defined as:

$$TETI = \frac{\int_0^t (4)^{TI(t')} dt'}{N}, \tag{11}$$

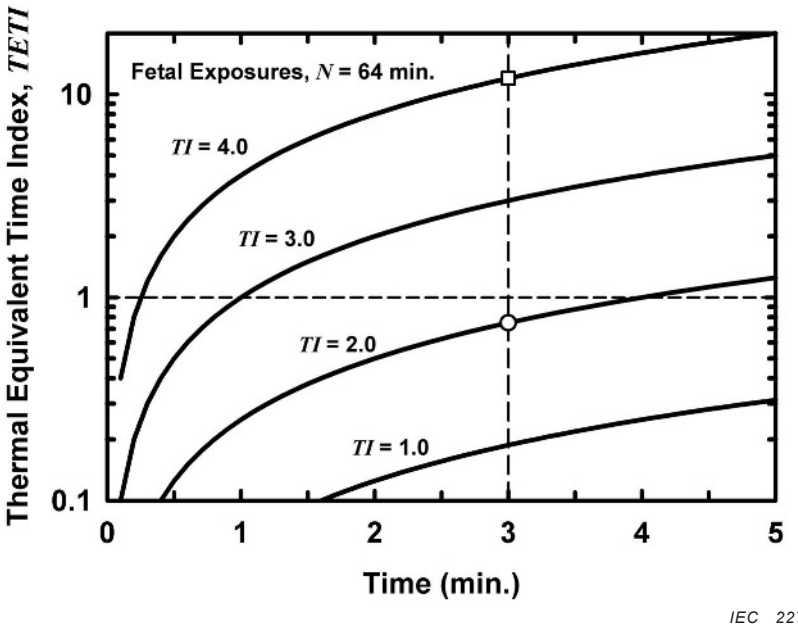
where t is now the total duration of the examination and t' is the duration at any particular value of TI. If the number of changes in TI is small, Equation (11) can be evaluated by a summation:

$$TETI = \frac{\sum_{i=1}^{n} (4)^{TI_i} \cdot \Delta t_i}{N}, \tag{12}$$

where n is the total number of values of TI used during the examination.

5.3.2 Illustrative results for the *TETI*

The values of **thermal equivalent time index** as a function of exposure duration to the foetus are shown in Figure 5 for values of the thermal index equal to 1,0, 2,0, 3,0 and 4,0. The plot shows that the $TETI$ increases exponentially with temperature, *i.e.*, with TI, where each curve for the next higher value of TI being displaced upward by a factor of 4 above the preceding curve. The functional dependence on time is linear, although this may be difficult to appreciate on this semi-logarithmic plot.



The open circle indicates that a 3 min exposure at TI = 2,0 will result in a $TETI$ of 0,75, while the open square shows that raising the TI to 4,0 will produce a $TETI$ of 12,0 for the same exposure duration.

Figure 5 – Thermally equivalent time index (solid curves) vs foetal exposure duration for TI = 1, 2, 3 and 4

An example of how the $TETI$ might be used is also shown in Figure 5. If an ultrasound examination of the foetus were performed in which the TI was held constant at 2 throughout the examination, and if the duration of the examination were 3 min, the $TETI$ would be computed as:

$$TETI = (4)^2 \cdot 3\,\text{min} / 64\,\text{min} = 0{,}75 \ . \tag{13}$$

This value is plotted as the open circle on the curve labelled "TI = 2,0" in Figure 5. Since 0,75 is less than 1,0, this examination exposed the foetus to very little, if any, risk of a thermally induced adverse effect. However, if the TI had been 4,0 rather than 2,0, and the duration had been the same, i.e., 3 min, then:

$$TETI = (4)^4 \cdot 3\,\text{min} / 64\,\text{min} = 12{,}0 \ . \tag{14}$$

This value is plotted as the open square in Figure 5. Because 12,0 is considerably greater than 1,0, there is the possibility of a thermally induced adverse effect.

It is also worth pointing out the conservative nature of the index in terms of the exposure duration in foetal examinations required to produce an index value of 1. These times are shown in Table 2. Of course the values in Table 2 are not meant to be interpreted as limiting the duration of an ultrasound examination. In ultrasonic scanning, the motion of the transducer would expose different tissues to varying shorter durations. In this situation, the $TETI$ would overestimate the true risk, and greater values of $TETI$ would be acceptable. However, because of the higher risk, it is advisable to limit a continuous stationary exposure of the foetus at a given TI value to the time specified in Table 2.

The corresponding durations to produce $TETI$ = 1 for non-foetal exposures are given in Table 3. The durations are greater than those shown in Table 2 by a factor of 16, consistent with the greater resistance to thermal insult of non-foetal tissue.

Table 2 – Foetal exposure durations for a thermally equivalent time index value of 1

Thermal index	0,5	1,0	1,5	2,0	3,0	4,0	5,0
Duration (min.)	32,0	16,0	8,0	4,0	1,0	0,25	0,0625

Table 3 – Non-foetal exposure durations for a thermally equivalent time index value of 1

Thermal index	0,5	1,0	1,5	2,0	3,0	4,0	5,0
Duration (min.)	512,0	256,0	128,0	64,0	16,0	4,0	1,0

5.3.3 Advantages of the *TETI*

Perhaps the most significant feature of the **thermally equivalent time index** is that it follows the same functional form as the **thermally equivalent time** itself but without requiring a major increase in the computational overhead of a diagnostic scanner. The *TETI* retains all of the previous work underlying the current **thermal index** plus any improvements to the temperature-estimation algorithms while offering several significant advantages:

- Both the thermal and temporal dependencies of the *TETI* are equivalent to those of the **thermally equivalent time**, which have been verified by numerous experimental results at all levels of biological organization from individual cells to tissues to whole organisms.
- The value displayed onscreen would be directly proportional to the probability of a thermally induced adverse event. That is, *TETI* normalizes the rate of induction of an adverse event to a specific reference rate, both in the form of the **thermally equivalent time**. The reference chosen depends on the tissue being exposed to the diagnostic ultrasonic field.
- Significantly, when *TETI* = 1, the exposure is approaching a level for which the probability of inducing an adverse thermal event is non-trivial. This provides a convenient reference point in the display for sonographers to use during the course of a diagnostic examination.
- After a sonographer becomes familiar with the *TETI*, it could provide a convenient and intuitive guide to the maximum duration of “safe” imaging of a given region of interest at a particular output level because the form of the expression for *TETI* is the same as the expression for the **thermally equivalent time**. In this case, “safe” is used in a relative rather than an absolute sense, and the term is interpreted as meaning “no more hazardous than” imaging at the reference output level.
- Because the *TETI* requires only a modest increase in computations, the changes to current software that are required for its implementation are also quite modest. Therefore, it may be possible to introduce the *TETI* into both current and future diagnostic scanners relatively quickly.

5.3.4 Shortcomings of the *TETI*

Because the proposed formulation for the *TETI* incorporates the *TI* directly, it is subject to some of the same limitations as the **thermal index**:

- Nonlinear propagation may occur when the acoustic path contains a significant amount of fluid or other low-attenuation material. The effect increases with output, and because *TETI* assumes linear propagation, this can introduce significant error into the calculation for intensity [3]. Technical specification IEC 61949 provides a method for minimizing these finite-amplitude effects when they occur during the calibration procedures for diagnostic transducers and suggests a method for estimating *in situ* exposure. However, use of this method is not currently required when making measurements of the physical quantities needed to determine the *TI*-value.
- Because *TETI* incorporates the *TI*, the *TETI* is based on the steady-state **temperature rise** calculated for long-duration exposures from a stationary transducer.

- Because *TETI* incorporates the *TI*, the *TETI* provides an estimate of risk at a location that may or may not coincide with the region of interest, an effect that may be of particular concern when the foetus is involved.
- It is well known that different **thermally equivalent times** are required for induction of different adverse events [21]. The *TETI* lacks the ability to quantify risk in absolute terms. This is perhaps its most significant failure.

5.4 Replacement of the *TI* with the time to threshold (*TT*)

5.4.1 Theory

As noted above in 4.2.2 and 5.2.4, the *TI* is proportional to the equilibrium **temperature rise** produced in a region of tissue by absorption of the acoustic beam. It is stated in Annex CC of IEC 60601-2-37, that the *TI* "gives a relative indication of the potential for **temperature [rise]** at a specific point along the ultrasound beam" and therefore that the *TI* provides "an indication of the conditions that are more likely than others to produce thermal… effects." However, as discussed in 3.2.1, the duration of exposure is a critical factor in determining the likelihood of inducing an adverse biological effect, and the *TI* ignores the time course of the temperature rise. To begin to overcome this shortcoming of the *TI*, a new safety parameter that quantifies the time required for the exposed tissue to reach a **temperature rise** equal to the **threshold temperature** for induction of an adverse event was proposed [8]. The proposed "**time to threshold**" (*TT*) display would have dimensions of time. Such a display would be easy for the user to understand and implement, the interpretation being that the user should not expect to image the same tissue for longer than the displayed *TT* without harm to the patient.

The implementation of *TT* requires a relatively accurate estimation of the increase in tissue temperature as a function of time $\Delta T(t)$ at the point of interest. This is accomplished by integrating the point-source solution to the bioheat transfer equation [2], [31], which gives the **temperature rise** produced at an arbitrary point (x_0, y_0, z_0) by a volume element dv located at a distance r and heated at a rate q_v:

$$\Delta T = \frac{q_v dv}{8\pi K r}\left\{E\left[2-\operatorname{erfc}\left(t^*-R\right)\right]+E^{-1}\operatorname{erfc}\left(t^*+R\right)\right\}. \tag{15}$$

In this equation, K is the thermal conductivity, $E=\exp\left(-r/L\right)$, $t^*=\sqrt{\left(t/\tau\right)}$, and $R=r\Big/\sqrt{\left(4\kappa t\right)}$, where the perfusion length $L=1\Big/\sqrt{\left(\kappa\tau\right)}$, κ is the thermal diffusivity, and τ is the perfusion time constant. The mathematical operation indicated by "erfc" is the complementary error function, defined as $\operatorname{erfc}(x)=1-2\int_0^x \exp\left(-y^2\right)dy\Big/\sqrt{\pi}$. The integration is carried out over a series of spherical shells around a sphere of radius r_{core} centered on the point of interest. To a good approximation, the solution is:

$$\Delta T(t)=\frac{\mu}{4\pi K}\left[2\pi\exp\left(-2\alpha z_0\right)I\left(x_0,y_0,z_0\right)r_{\text{core}}^2+\int_{r_{\text{core}}}^{\infty}\frac{\left\{E\left[2-\operatorname{erfc}\left(t^*-R\right)\right]+E^{-1}\operatorname{erfc}\left(t^*+R\right)\right\}}{r}\right.$$

$$\left.\left(\int_{-r}^{r} r\exp\left(-2\alpha z\right)\left(\int_0^{2\pi} I(x,y,z)d\varphi\right)dz\right)dr\right], \tag{16}$$

where μ is the **acoustic absorption coefficient**, α is **acoustic attenuation coefficient** for pressure and I is the temporal average intensity in water (which is implicitly assumed to be linear and non-attenuating); the heating rate $q_v = 2\mu I$.

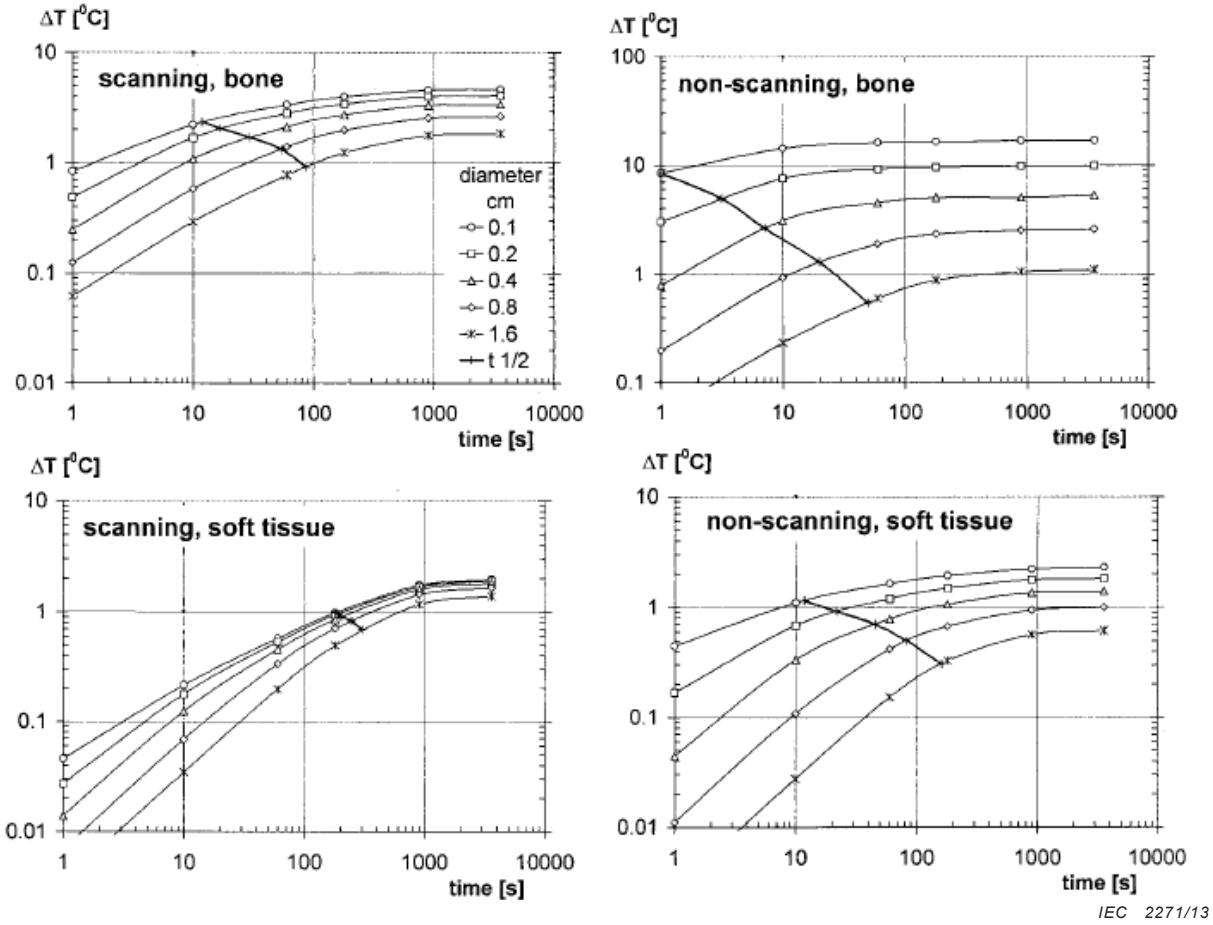
5.4.2 Illustrative results for the TT

Although a complete set of calculations for even one type of transducer, e.g., a single circular element or a linear phased array, is not yet available, representative calculations for two tissue types, soft tissue and bone, and for both **scanning** and **non-scanning imaging modes** have been presented [8]. To facilitate comparison with results for the models used with the TI, the values of several parameters were taken to be the same as in model H.3: heat capacity = 4,16 $\times$ 10^6 J m^{-3} K^{-1}, thermal conductivity = 0,6 W m^{-1} K^{-1}, thermal diffusivity = 0,14 mm^2 s^{-1}, perfusion time constant = 720 s, and perfusion length = 1,02 cm. The soft-tissue **acoustic attenuation coefficient** was taken as 1 dB cm^{-1}, or 0,115 Np cm^{-1}, corresponding to the attenuation coefficient that would be found in model H.3 assuming an acoustic frequency of 3,3 MHz (0,3 dB cm^{-1} MHz^{-1} $\times$ 3,3 MHz = 1 dB cm^{-1}). The calculations for bone assumed absorption of 50% of the impinging energy in a thin (1 mm thick) sheet, with the remaining 50% reflected back into the overlying soft tissue. The **temperature rise** was calculated in the middle of the bone layer, and the heating of the surrounding soft tissue was ignored; the thermal and perfusion properties of the bone were set equal to those of the soft tissue.

For the **non-scanning mode** beam, a homogeneous cylindrical geometry was assumed. The intensity in the beam was assumed to be the power emitted by the transducer divided by the area of the beam; the intensity was zero outside the beam. Gaussian and Bessinc profiles were also investigated, although their effects on TT were generally small. Five beam diameters were studied: 0,1 cm, 0,2 cm, 0,4 cm, 0,8 cm and 1,6 cm. The exposure parameter used was the attenuated power $P_{\mathrm{a}} = P \exp(-2\alpha z_0)$, where P is the power emitted by the transducer.

For the **scanning mode** beam, scanning was assumed to be in a direction perpendicular to the beam axis over a distance of 8 cm. Further, it was assumed that a rectangular volume of length 8 cm and width equal to the beam diameter was uniformly insonated. Five beam diameters were studied: 0,1, 0,2, 0,4, 0,8 and 1,6 cm. The exposure parameter used was the attenuated bounded output power $P_{1\mathrm{a}} = P_1 \exp(-2\alpha z_0)$, where P_1 is the power emitted per cm of transducer width. For both **scanning** and **non-scanning mode** beams, the transducer face was considered to be adiabatic, i.e., that no heat flow occurred at the face.

For each of the four combinations of tissue model (soft tissue and bone in soft tissue) and exposure geometries (scanning and non-scanning), $\Delta T(t)$ was calculated for various depths of the point of interest for the same value of attenuated power. It was found that the **temperature rise** was smaller for locations closer to the transducer, but that beyond about 3 cm ($z_0 > 3$ cm), the maximum elevation was approximately constant. Calculations for $\Delta T(t)$ at $z_0 > 3$ cm and power parameters P = 100 mW and P_1 = 100 mW cm^{-1} are shown in Figure 6.

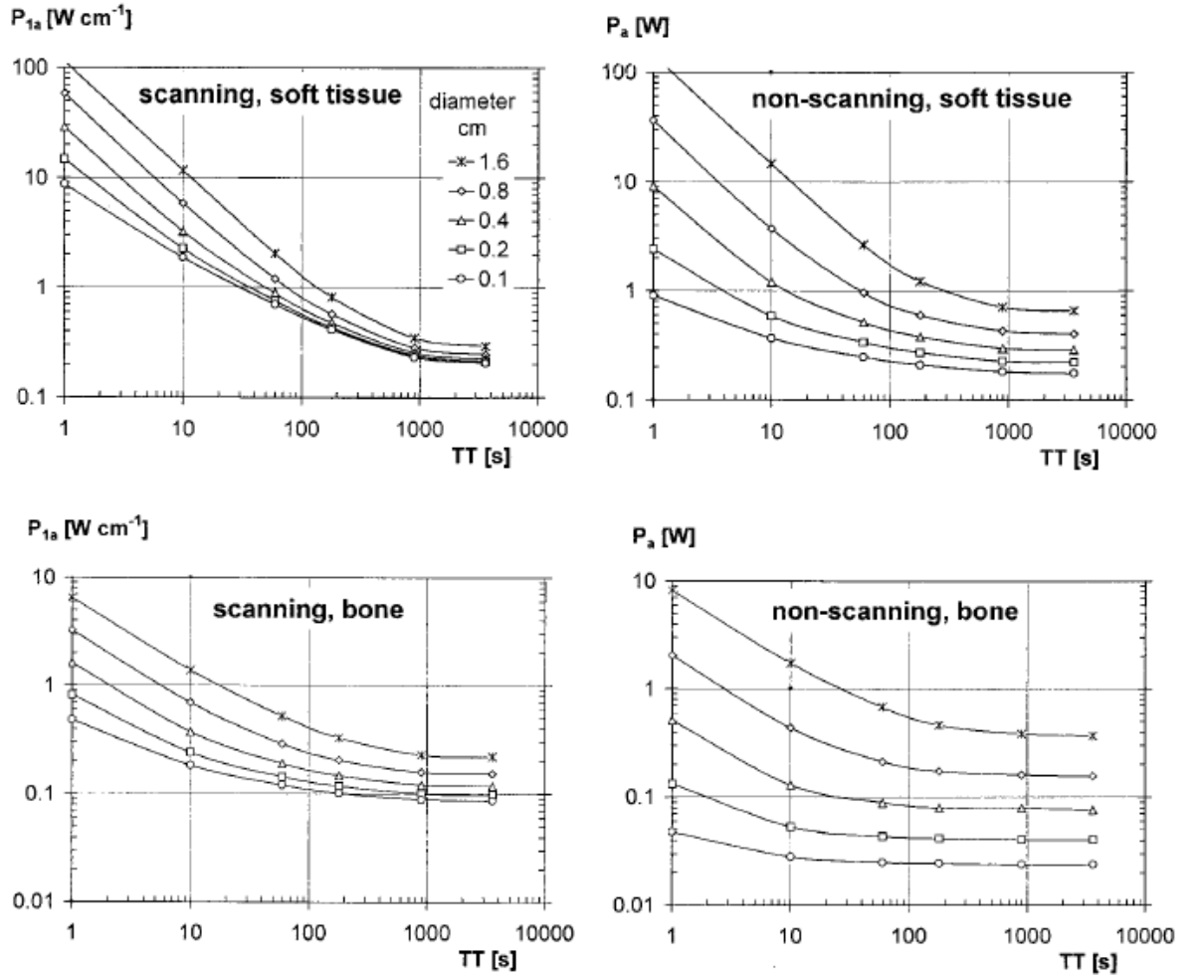


The five curves in each graph indicate five beam widths: 0,1 cm, 0,2 cm, 0,4 cm, 0,8 cm and 1,6 cm. The curve through the crosses indicates points, which are at 50% of the equilibrium temperature rise for that beam width. The non-scanning-mode graphs are for an attenuated power of 100 mW; the scanning-mode graphs are for an attenuated bounded power of 100 mW cm^{-1}; see [8].

Figure 6 – Temperature rise for distance (z_0 > 3 cm) for four models as a function of US exposure time

As would be expected, ΔT initially increases linearly and reaches a plateau at long exposure durations. The time required to reach the plateau is approximately the time needed to establish thermal equilibrium between the heat source and sink, i.e., between the heat generated by absorption of the acoustic field and the heat carried away by diffusion and perfusion; this time is on the order of the ratio of the square of the linear dimension of the source (e.g., the beam width) and the thermal diffusivity. The temperature elevations shown in Figure 6 are greater for bone than for soft tissue, reflecting the greater absorption in bone. ΔT is also greater for narrower rather than wider beams, a consequence of the higher local intensity for the combination of parameters chosen. It was also found that ΔT increases by ≤ 12 % for insonation times ≤ 180 s. Thus the effect of perfusion is relatively small for exposures less than about 3 min.

Because linear models were used to produce the graphs in Figure 6, the attenuated power at which the threshold temperature rise is reached after a given time for a given configuration may be easily calculated. For the non-scanning models $P_a = P_{a,ref} \Delta T_{thr} / \Delta T$, while for the scanning models $P_{1a} = P_{1a,ref} \Delta T_{thr} / \Delta T$, where P = 100 mW, P_1 = 100 mW cm^{-1} and ΔT_{thr} is the **threshold temperature rise**. The value of ΔT_{thr} appropriate for normothermic patients has been given as 4 °C in two reports [32], [33]. The results shown in Figure 7 have been computed assuming this value for ΔT_{thr}.

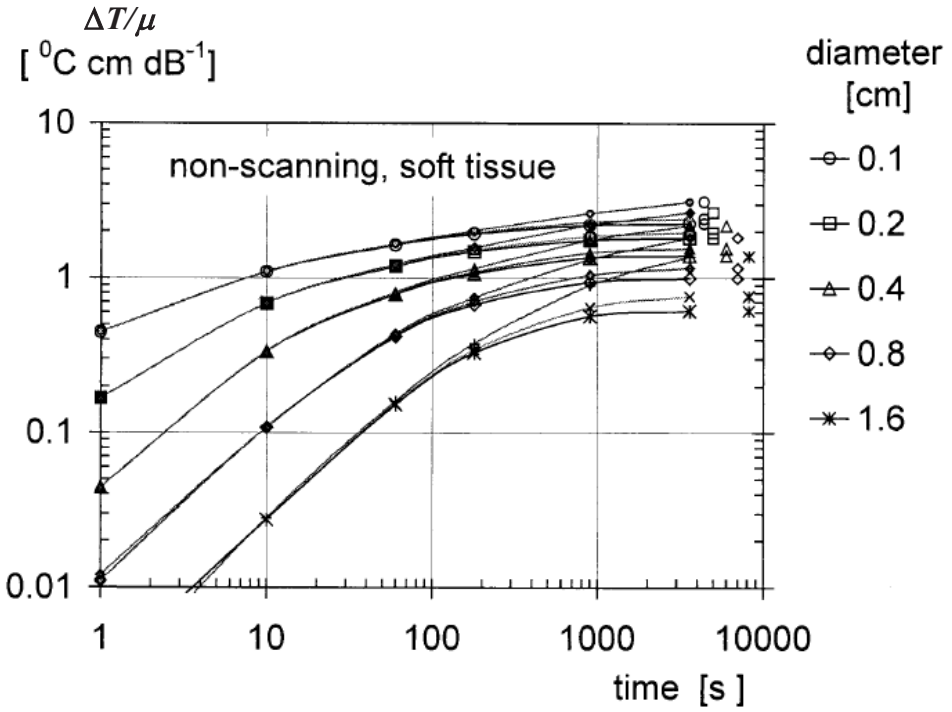


The relations were derived for five beam diameters in four models. The power parameters are attenuated power (P_a) for the non-scanning models and attenuated bounded power (P_{1a}) for the scanning models; see [8].

Figure 7 – Relation between TT (time to threshold) and power parameters that give a temperature rise of ΔT_{thr} = 4 °C

The exposure durations of practical interest are generally about 10 s to 1 000 s; this corresponds to the range of times required to establish thermal equilibrium in the models studied. Consideration of the results in Figure 7 indicates that the permissible output power level depends strongly on insonation time in many cases. For exposure durations of 10 s to 1 000 s, the range in the power parameter can be as much as a factor of 40 for a wide, scanning beam in soft tissue, or as small as a factor of 1,2 for a narrow, non-scanning beam impinging on bone.

To investigate the effect of non-local heating, the calculation of the heating of soft tissue by a non-scanning beam for **acoustic absorption coefficients** of 3 dB cm^{-1} and 5 dB cm^{-1} was investigated [8]. As expected from analytical theory, heating at short exposure times was proportional to the absorption coefficient. Therefore, the results were plotted as the ratio of **temperature rise** ΔT to the absorption coefficient in Figure 8. For exposure durations of up to 180 s, this relation is independent of absorption. For longer insonation times, the **temperature rise** is higher for higher values of absorption because *i*) heat sources at greater distance contribute and *ii*) at higher absorption rates, the effect of additional heat deposition in front of the point of interest surpasses the effect of diminished heat deposition beyond the observation point. A similar result was found for a scanning beam in soft tissue. Note that this calculation does not consider the increased cooling due to the increase in tissue perfusion expected at higher temperatures.



For each beam diameter, three values of the absorption coefficient were studied: 1 dB cm^{-1}, 3 dB cm^{-1} and 5 dB cm^{-1}. To distinguish the end points after 1 h, they have been plotted once more in separate columns on the right side of the graph; see [8].

Figure 8 – The ratio of temperature rise to acoustic absorption coefficient, $\Delta T/\mu$, vs exposure duration for the non-scanning soft tissue model with P_a = 100 mW.

5.4.3 Advantages of the *TT*

Replacement of the *TI* with the *TT* offers the following advantages:

- The value displayed onscreen would be dimensional, having units of time. It would therefore be extremely simple for the user to interpret and implement in real time. The user would simply be told that it is potentially dangerous to continuously scan the same tissue for a time greater than *TT*.
- The use of *TT* permits the use of higher output levels, at least for short imaging durations. Higher powers often improve image quality, particularly for deep tissues imaged in harmonic mode and for Doppler techniques.
- The *TT* offers a more direct indication of risk to the patient. If the duration of imaging is less than *TT*, and assuming that the same tissue has not been scanned multiple times in a short period, then it may be concluded that the risk to the patient is at least very small, possibly nonexistent.
- The *TT* concentrates on shorter exposure durations, and thus is less susceptible to the effects of cooling by blood perfusion than is the *TI*.

5.4.4 Shortcomings of the *TT*

Replacement of the *TI* with the *TT* is subject to the following limitations:

- The *TT* and *TI* share the same basic model for tissue heating. Thus both parameters have the same problems in attempting to estimate *in vivo* **temperature rise** from average, or worst-case, values for important physical factors such as **acoustic absorption** and **attenuation coefficients**, insertion loss, thermal conductivity, heat capacity and perfusion length.

- Nonlinear propagation may occur when the acoustic path contains a significant amount of fluid or other low-attenuation material. The effect increases with output, and because TI_{cur} assumes linear propagation, this can introduce significant error into the calculation for intensity [3]. Technical specification IEC 61949 provides a method for minimizing these finite-amplitude effects when they occur during the calibration procedures for diagnostic transducers and suggests a method for estimating in situ exposure. However, use of this method is not currently required when making measurements of the physical quantities needed to determine the *TI*-value.
- Depending on its method of implementation, the TT may provide an estimate of risk at a location that does not coincide with the region of interest, an effect that may be of particular concern when the foetus is involved.
- There is no generally accepted **threshold temperature rise** for induction of any particular effect. In addition, the existence of a temperature threshold is not firmly established.

  The TT is a relatively new concept. It will require considerable effort to demonstrate that its underlying principle is applicable to the ultrasonic fields generated by actual clinical transducers. As part of the needed studies, it will be desirable to consider the optimal method for implementing the TT as a real-time display.

5.5 Replacement of the *TI* with the safe use time (*SUT*)

5.5.1 Theory

Although tissue that attains a specified **threshold temperature rise** may be at risk for thermal injury, it will not necessarily actually exhibit damage unless the specified **temperature rise** has persisted for a specified duration of time. If the source of heating is removed so that the **threshold temperature rise** is not maintained long enough, then no thermal injury will result. The mathematical approach may be thought of as a combination of those described in 5.2.1 and 5.3.1, plus a unique extension to encompass the required duration of heating. The following is taken from [16].

As noted in 5.2.1, for two different **temperature rises**, ΔT_1 and ΔT_2, both functions of time, there will be two different increases in the incidence of a specified biological effect. From Equation (5), the ratio of the corresponding increases in rates ΔIR_1 and ΔIR_2, is:

$$\frac{\Delta IR_2}{\Delta IR_1} = \frac{\dfrac{1}{t_h}\displaystyle\int_0^{t_h} R^{\Delta T_2 / C_T}\, dt - 1}{\dfrac{1}{t_h}\displaystyle\int_0^{t_h} R^{\Delta T_1 / C_T}\, dt - 1} = \frac{\displaystyle\int_0^{t_h} R^{\Delta T_2 / C_T}\, dt - 1}{\displaystyle\int_0^{t_h} R^{\Delta T_1 / C_T}\, dt - 1}, \tag{17}$$

where the constant C_T = 1 °C and t_h is the duration of heating.

The threshold temperature-time combination was chosen to be a **temperature rise** of 4 °C for 4 min, or 240 s [16], [34]. Assuming $\Delta T_1 < 6$ °C allows R to be set equal to 4. For an ultrasound examination that produces a temperature profile of $\Delta T_1(t)$, that also produces a level of biological effect equal to this reference exposure, the following equation must hold:

$$\int_0^{240\,\mathrm{s}} 4^4\, dt - 240\,\mathrm{s} = \int_0^{t_h} 4^{\Delta T_1(t) / C_T}\, dt - t_h = \int_0^{SUT} 4^{\Delta T_1(t) / C_T}\, dt - SUT, \tag{18}$$

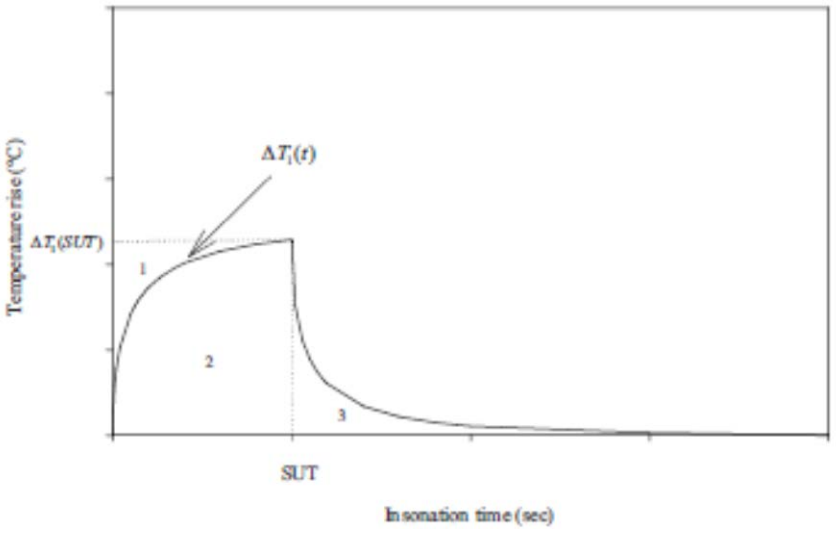
where t_h, i.e., the **safe use time**, SUT, is now the duration of scanning that would be no more hazardous than scanning at the reference output level. The left-hand side of Equation (18) can be evaluated immediately, yielding:

$$61\,200\,\mathrm{s} = \int_0^{SUT} 4^{\Delta T_1(t)/C_T}\,dt - SUT \quad . \tag{19}$$

Solution of Equation (19) gives the value of the **safe use time** for an exposure condition that produces heating of $\Delta T_1(t)$. However, the calculation given in Equation (19) requires an integration that causes a computational burden. The calculation can be simplified by using the **temperature rise** value at the end of SUT, i.e., $\Delta T_1(SUT)$:

$$61\,200\,\mathrm{s} = SUT \times 4^{\Delta T_1(t)/C_T} - SUT \quad . \tag{20}$$

This is illustrated in Figure 9, which shows a typical example of **temperature rise** induced by an ultrasonic wave at a representative point in the beam. Areas 2 and 3 under the curve are, respectively, the contributions to the integral in Equation (19) during the heating and cooling periods. The contributions of the **temperature rise** during both the heating and cooling periods have to be taken into account in the calculation of the relative increase in the incidence rate. While Equation (19) considers the sum of the contributions of areas 2 and 3, Equation (20) takes into account the sum of the contributions of areas 1 and 2. High temperatures are present for a longer time in area 1 than in area 3. Therefore, Equation (20), results in an additional safety margin because area 3 contributes less to the total **thermally equivalent time** than area 1 [16].



IEC 2274/13

The examination is terminated when $t = SUT$. The temperature rise in tissue at $t = SUT$ is $\Delta T_1(SUT)$.

Figure 9 – A typical example of temperature rise due to diagnostic ultrasound

To provide a relatively simple method for producing the curves for **temperature rise** needed to implement Equation (20), The axial temperature-rise profiles for a series of 96 combinations of acoustic frequency (f = 1, 3, 5, 7, 9 and 11 MHz), source diameter (D = 1, 2, 3 and 4 cm) and focal length, F, such that transducer f-numbers of 1, 2, 3 and 4 were studied [16] using the model described in [8], described in 5.3. In each case, the acoustic output power, W, was chosen to obtain $I_{SPTA.3}$ = 720 mW cm^{-2}. They then fit the resulting data at the location of the **temperature rise**, ΔT_{max}, to an equation of the form:

$$\Delta T(t) = \Delta T_{max} X(t) = \Delta T_{max}\left[1 - \exp\left(-\sqrt{t/a}\right)\right], \tag{21}$$

where a is the inverse of the rate constant describing the rate of change in the temperature, see Figure 9. The data for ΔT_{max} and a are normalized to C_T (= 1 °C) and 1 s, respectively, and then fit to the following expressions:

$$\frac{\Delta T_{max}}{C_T} = A W_n^b f_n^c D_n^d F_n^f , \tag{22a}$$

$$\frac{a}{1\,s} = E f_n^g D_n^h F_n^i , \tag{22b}$$

where A, E and b, c, d, f, g, h, i are constants to be determined by the fitting routine, W_n = W / 1 mW, f_n = f / 1 MHz, D_n = D / 1 cm, and F_n = F / 1 cm. The resulting expression is:

$$\Delta T(t) = \frac{W_n^{1,029} f_n^{0,580}}{78{,}52 D_n^{0,497} F_n^{0,614}} \left[1 - \exp\left(- \sqrt{\frac{D_n^{1,127} f_n^{0,581} t}{(25{,}2\,s) F_n^{1,228}}} \right) \right] °C . \tag{23}$$

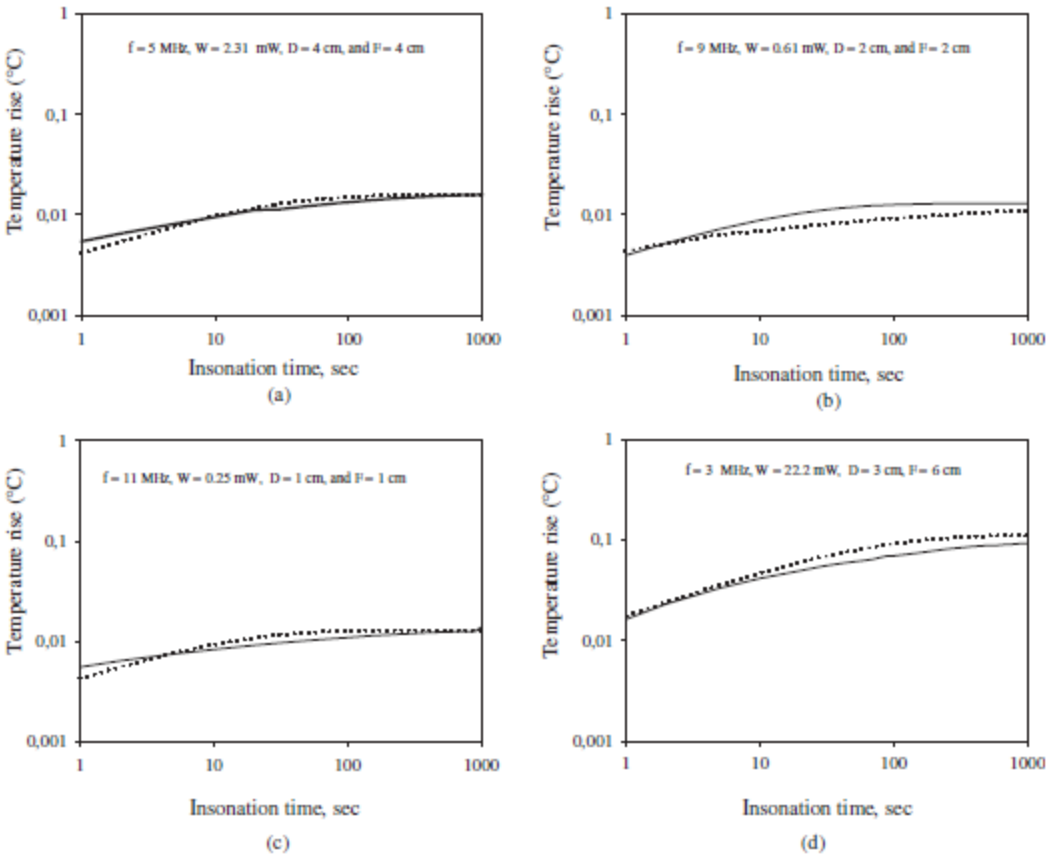
5.5.2 Illustrative results for the *SUT*

The values of **temperature rise** as a function of insonation time predicted using Equations (16) and (23), respectively, are shown in Figure 10 for the case of a **non-scanning** imaging **mode**. Satisfactory agreement is obtained for these exposure conditions. It is not possible to present the results for all exposure conditions, but the same trends are exhibited in other cases.

To evaluate the effects of accuracy of the prediction for **temperature rise**, i.e., Equation (23), and the worst-case assumption on the calculations, the **thermal load**, TL, is defined as [16]:

$$TL = t \times 4^{\Delta T_1(t)/C_T} - t . \tag{24}$$

Curves for TL under 12 exposure conditions as a function of t and f-number are shown in Figure 11. The insonation time at which a TL curve for a given case intersects the “61 200 s” line is the SUT value for that case, see Equation (20). Satisfactory agreement between the TL curves calculated for the two equations for predicting **temperature rise** is obtained except for short exposure times (for example, below 1 000 s). These discrepancies are observed because of the worst-case assumption discussed in 5.3.1. Although there is a relatively higher error in the prediction of the lower ΔT_{max}, the SUT values predicted in the two cases for the corresponding exposure conditions are almost equal to each other (e.g., Figure 11(a), f-number = 1). However, the prediction error for the higher ΔT_{max} values (e.g., above 3 °C) is more important compared to that of the lower ΔT_{max} during the calculation of the SUT (Figure 11(b), f-number = 4, ΔT_{max} = 3,414 °C). Therefore, the use of an additional safety margin is required, because the prediction is not on the safe side for all cases to which it can be applied. To examine the effect of the time dependency on the variability of the SUT, the calculation above was repeated under the assumption that ΔT_{max} is achieved instantaneously, intentionally ignoring the contribution of temperatures lower than ΔT_{max}. Table 4 shows the results from those calculations for four exposure conditions. These results suggest no significant difference between corresponding SUT values when the maximum **temperature rise** <3 °C. However, ignoring the contribution during the interval at lower temperature substantially affects the SUT value when the maximum **temperature rise** is >3 °C.



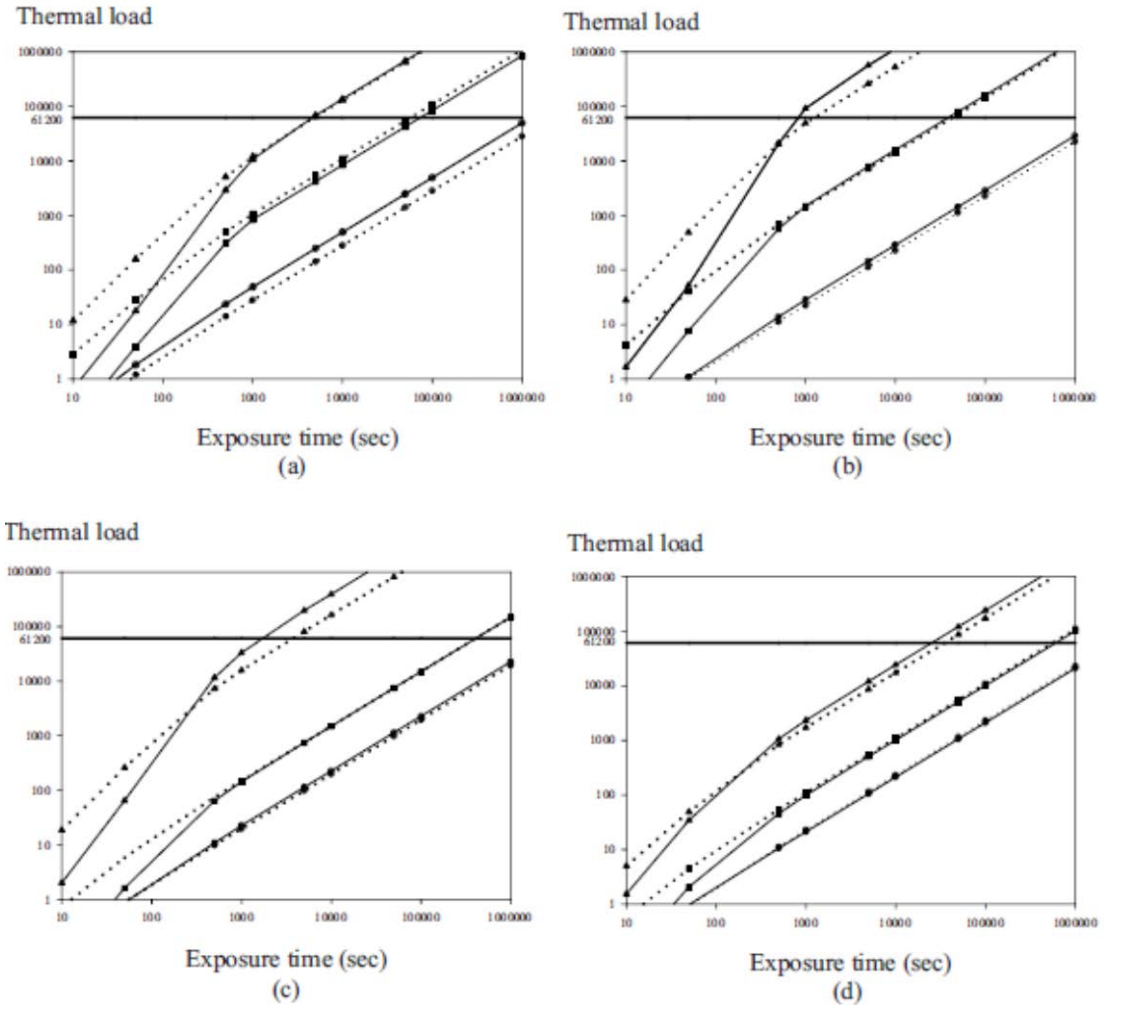
(a) f = 5 MHz, W = 2,31 mW, D = 4 cm, and F = 4 cm; (b) f = 9 MHz, W = 0,61 mW, D = 2 cm, and F = 2 cm; (c) f = 11 MHz, W = 0,25 mW, D = 1 cm, and F = 1 cm; and (d) f = 3 MHz, W = 22,2 mW, D = 3 cm, and F = 6 cm. The solid and dotted lines give the values calculated using Equations (16) and (23), respectively; see [16].

Figure 10 – Values of temperature rise as a function of insonation time

As for the TT, the SUT model makes it possible to operate a diagnostic ultrasound machine at an output power, W_a, much higher than the maximum power, W, currently permitted under the FDA condition $I_{SPTA.3} < 720$ mW cm^{-2} for a desired brief exposure time to provide better imaging quality while staying within safe limits. For example, assume that the user of a diagnostic scanner wants to examine a region of interest for an exposure time of 500 s; hence SUT is selected as 500 s. Incorporating that value of SUT into Equation (20) leads to the following expression:

$$61\,700 \text{ s} = 4^{\Delta T_1(500 \text{ s})/C_T} \times 500 \text{ s} \ . \tag{25}$$

For four exposure conditions, Table 5 summarizes the corresponding power W, the observed and predicted values of a maximum **temperature rise** due to these conditions, and W_a values for SUT = 500 s. These results suggest that the agreement between the values calculated for W_a using Equations (16) and (23) for a given exposure condition is generally satisfactory. However, the TL value for a **temperature rise** calculated using Equation (23) is higher than that for the same **temperature rise** calculated using Equation (16) for a case in which a deep focus is present because of the approach used in the determination of ΔT_{max} and $X(t)$ makes use of the result that the location of ΔT_{max} moves toward the acoustic source as the f-number increases [35]. Therefore, the proposed **temperature rise** model can conservatively calculate W_a for such a case (Table 5). The variability in the models at short exposure times has a substantial effect on the calculation of W_a because it is necessary to focus on short exposure times when the operator wants to use higher acoustic output power. Therefore, the present SUT model can be applied for brief exposure times, even lower than the reference exposure time (240 s), provided an accurate model of the **temperature rise** is available.



(a) f = 3 MHz and D = 4 cm, (b) f = 5 MHz and D = 3 cm, (c) f = 7 MHz and D = 2 cm, and (d) f = 9 MHz and D = 1 cm. The solid and dotted lines give the values calculated using Equations (16) and (23), respectively. The symbols ●, ■, and ▲ indicate f-number = 1, f-number = 3, and f-number = 4, respectively; see [16].

Figure 11 – The thermal load as a function of time and f-number

Table 4 – SUT values when including and ignoring the contribution of temperatures lower than ΔT_{max} for the four exposure conditions and the corresponding values of ΔT_{max}

Exposure condition	SUT when including the contribution at lower temperature (s)	SUT when ignoring the contribution at lower temperature (s)	ΔT_{max} (°C)
f = 3 MHz, D = 4 cm, f-number = 4	4 750	4 740	1,902
f = 5 MHz, D = 3 cm, f-number = 4	1 200	1 150	2,869
f = 9 MHz, D = 3 cm, f-number = 3	495	455	3,538
f = 7 MHz, D = 4 cm, f-number = 3	200	109	4,570

Table 5 – Values of W, W_a, and ΔT_{max} for the case of SUT = 500 s.

Exposure condition	W (mW)	W_a Eq. (9) (mW)	W_a Eq. (16) (mW)	ΔT_{max} Eq. (9) (°C)	ΔT_{max} Eq. (16) (°C)
f = 3 MHz, D = 4 cm, f-number = 4	712	1 792	1 424	1,932	1,902
f = 5 MHz, D = 3 cm, f-number = 3	115,9	738	647	0,682	0,642
f = 7 MHz, D = 2 cm, f-number = 1	0,77	173	190	0,016	0,014
f = 9 MHz, D = 1 cm, f-number = 1	0,33	72	76	0,016	0,015

5.5.3 Advantages of the SUT

Replacement of the TI with the SUT offers the following advantages:

- The value displayed onscreen would be dimensional, having units of time. It would therefore be extremely simple for the user to interpret and implement in real time. The user would simply be told that it is potentially dangerous to continuously scan the same tissue for a time greater than SUT.
- The use of SUT permits the use of higher output levels, at least for short imaging durations. Higher powers often improve image quality, particularly for deep tissues imaged in harmonic mode and for Doppler techniques.
- The SUT offers a more direct indication of risk to the patient. If the duration of imaging is less than SUT, and assuming that the same tissue has not been scanned multiple times in a short period, then it may be concluded that the risk to the patient is at least very small, possibly nonexistent.

5.5.4 Shortcomings of the SUT

Replacement of the TI with the SUT is subject to the following limitations:

- The SUT, TT and TI share the same basic model for tissue heating. Thus these parameters all have the same problems in attempting to estimate *in vivo* **temperature rise** from average, or worst-case, values for important physical factors such as **acoustic absorption** and **attenuation coefficients**, insertion loss, thermal conductivity, heat capacity and perfusion length.
- Nonlinear propagation may occur when the acoustic path contains a significant amount of fluid or other low-attenuation material. The effect increases with output, and because TI_{cur} assumes linear propagation, this can introduce significant error into the calculation for intensity [3]. Technical specification IEC 61949 provides a method for minimizing these finite-amplitude effects when they occur during the calibration procedures for diagnostic transducers and suggests a method for estimating in situ exposure. However, use of this method is not currently required when making measurements of the physical quantities needed to determine the TI-value.
- Depending on its method of implementation, the SUT may provide an estimate of risk at a location that does not coincide with the region of interest, an effect that may be of particular concern when the foetus is involved.
- There is no generally accepted **threshold temperature rise** for induction of any particular effect. In addition, the existence of a temperature threshold is not firmly established.
- The SUT is a relatively new concept. It will require considerable effort to demonstrate that it is applicable to the ultrasonic fields generated by actual clinical transducers. As part of the needed studies, it will be desirable to consider the optimal method for implementing the SUT as a real-time display.

5.6 Replacement of the *TI* with the thermally equivalent time displayed (*TETD*)

5.6.1 Theory

Because the value of the **threshold temperature rise** for any particular tissue in humans is not known, and indeed because there is not agreement even as to the very existence of such a threshold, an alternative, related method of analysis is outlined here. The same mathematical approach described in Equations (15) and (16) may be used. However, rather than employ a threshold for which either very limited or no data exist, the **thermally equivalent time** will be calculated directly from the time-temperature profile obtained from Equation (16), see [36].

As noted in 5.2.1, the **thermally equivalent time** (t_{43}) relates the exposure time t_1 required to produce a given level of effect at one temperature $T(t)$ to the time required to produce the same level of effect, termed an 'isoeffect', at a reference temperature of 43 °C. In this way, the expression for t_{43} can relate a thermal exposure with any arbitrary time-temperature profile $T(t)$, to an equivalent exposure for a time t_{43} at a constant temperature of 43 °C:

$$t_{43} = \int_0^{t'} R^{\,[T(t)-43\,^\circ\mathrm{C}]/C_\mathrm{T}}\, dt \tag{26}$$

Note that the value chosen for the reference temperature may vary with the endpoint of interest (56 °C is sometimes chosen in thermal ablation studies) as well as with the species being studied. In humans, for hyperthermia exposures the reference temperature is 43 °C.

The **thermally equivalent time** concept provides a relatively simple means of quantifying the thermal damage produced by a heating-cooling cycle having an arbitrary time-temperature profile. For example, an exponential temperature rise provides a convenient, approximate solution to the bio-heat transfer equation for ultrasound-exposed tissue. The equation is $T(t) = T_\mathrm{o} + \Delta T_\mathrm{max}\left(1 - e^{-k_\mathrm{T} t}\right)$, where T_o is the normal physiologic temperature, ΔT_max is the maximum, or steady-state temperature increase, k_T is the rate constant for temperature increase, and t is the time elapsed since the beginning of the exposure. The time required for the temperature increase to reach half of its final value, $t_{1/2}$, is 0,693/k_T. Since the reference temperature may be written as $T_\mathrm{REF} = 43\ ^\circ\mathrm{C} = T_\mathrm{o} + \Delta T_\mathrm{REF} = T_\mathrm{o} + 6\ ^\circ\mathrm{C}$, Equation (26) may be approximated as:

$$t_{43} = \sum_{i=0}^{n} \left\langle R^{\left[\Delta T_\mathrm{max}\left(1-e^{-k_\mathrm{T} t_i}\right)-6\,^\circ\mathrm{C}\right]/C_\mathrm{T}} \right\rangle \Delta t_i = R^{(\Delta T_\mathrm{max}-6\,^\circ\mathrm{C})/C_\mathrm{T}} \sum_{i=0}^{n} \left\langle R^{-\Delta T_\mathrm{max} e^{-k_\mathrm{T} t_i}/C_\mathrm{T}} \right\rangle \Delta t_i\,, \tag{27}$$

where $< >$ indicates the time-average over the interval Δt_i. This form of the **thermally equivalent time** is well-suited to computation, requiring only the addition of a single term to the summation for each successive time step. Note that the important parameter in the expression is ΔT_REF, and not T_REF itself. Thus it is the temperature rise above a patient's normal core temperature that must be considered when estimating **thermally equivalent time**.

In calculations of the **thermally equivalent time**, it is desirable to include the cool-down portion of a typical heating curve which must inevitably follow the preceding heating phase. Again assuming an exponential form, a second temperature rate constant, k_T2, quantifies the decrease in temperature following exposure:

$$T(t) = T_\mathrm{o} + \Delta T_\mathrm{max}\left(1 - e^{-k_\mathrm{T} t}\right), \quad t \le t_\mathrm{h}, \tag{28a}$$

$$T(t) = T_o + \Delta T_{max}\left(1 - e^{-k_T t_h}\right)e^{-k_{T2}(t-t_h)}, \quad t > t_h, \tag{28b}$$

where t_h is the duration of heating. The final form of the **thermally equivalent time** is then:

$$\begin{aligned} t_{43} &= \sum_{i=1}^{n}\left\langle R^{\left[\Delta T_{max}\left(1-e^{-k_T t_i}\right)-6\,°C\right]/C_T}\right\rangle \Delta t_i + \sum_{n+1}^{m}\left\langle R^{\left[\Delta T_{max}\left(1-e^{-k_T t_h}\right)e^{-k_{T2}(t_i-t_h)}-6\,°C\right]/C_T}\right\rangle \Delta t_i \\ &= R^{(\Delta T_{max}-6\,°C)/C_T}\sum_{i=1}^{n}\left\langle R^{-\Delta T_{max}e^{-k_T t_i}/C_T}\right\rangle \Delta t_i + \sum_{n+1}^{m}\left\langle R^{\left[\Delta T_{max}\left(1-e^{-k_T t_h}\right)e^{-k_{T2}(t_i-t_h)}-6\,°C\right]/C_T}\right\rangle \Delta t_i \end{aligned}, \tag{29}$$

where t_f is the time at which the temperature has returned to T_o; t_f may also be an arbitrarily selected maximum time.

Once the value for the **thermally equivalent time** has been determined from Equation (29), the probability that an adverse effect results from that thermal exposure is calculated. First, the damage rate constant k is determined at $T = T_{REF}$; $k(T_{REF}) = k_{REF}$ using the Eyring equation with the activation energy for the effect of interest:

$$k_{ref} = \frac{k_B T_{REF}}{h} e^{\Delta S/R_g} e^{-\Delta H/R_g T_{REF}} = A e^{-\Delta H/R_g T_{REF}} \approx A e^{-E_a/R_g T_{REF}}, \tag{30}$$

where k_B is Boltzmann's constant, h is Planck's constant, ΔG is the Gibbs free energy, and $\Delta G = \Delta H - T\Delta S$. Then the probability that an organism is affected is calculated from:

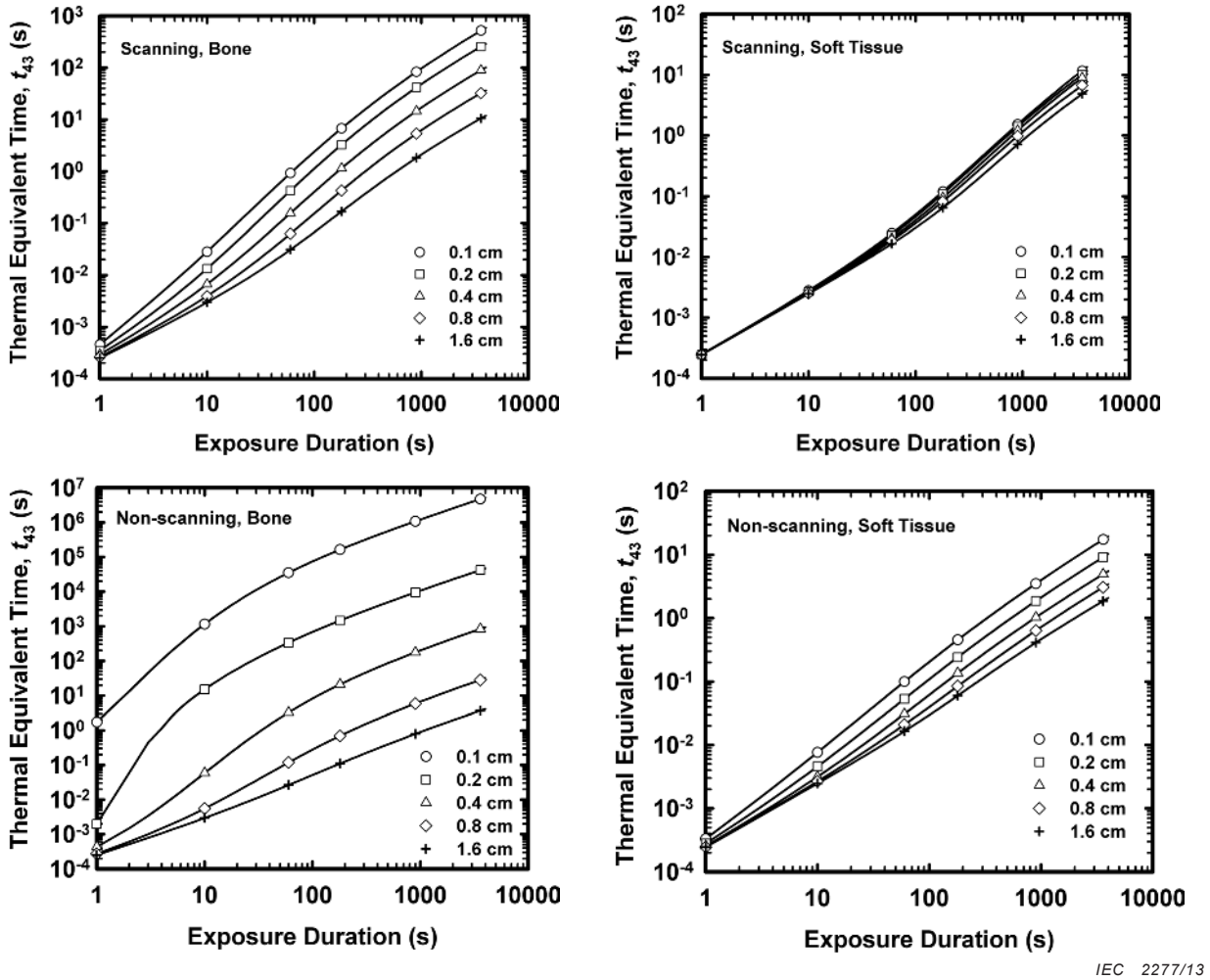
$$F(t) = \left(1 - e^{-k_{REF} t}\right)^{n_e}, \tag{31}$$

where the extrapolation number n_e is the number of discrete and independent events required to induce the effect. Note that the use of t_{REF} and k_{REF} simplifies calculations of the probability of damage for cell types having similar responses to thermal injury, i.e., similar values of E_a, although it is not necessary.

5.6.2 Illustrative results for the *TETD*

Thermally equivalent times corresponding to the temperature profiles shown in Figure 6 were computed to provide easy comparison of the two approaches (*TT* vs *TETD*). Because the profiles in Figure 6 do not fit the exponential form assumed in Equations (28) and (29), the data points were fit to logistic dose response curves; in all cases the correlation coefficient $r >$ 0,996. The **thermally equivalent times** (t_{43}) were calculated from the fits assuming R is 4 for $\Delta T \leq 6$ °C and R is 2 for $\Delta T > 6$ °C. For simplicity, the additional dose accumulated during the cooling phase of the exposure was ignored, resulting in a multiplicative error factor of at most 2.

The results for **thermally equivalent times** are shown in Figure 12. As would be expected, the values for bone are greater, and sometimes much greater, than for soft tissue. In fact, although the calculated temperature increases shown in Figure 6 for soft tissue and bone may differ by factors of 2 to 20, the corresponding **thermally equivalent times** differ by up to 100,000. This reflects the exponential nature of the physiological response to thermal exposure.



The relations were derived for five beam diameters in four models.

Figure 12 – A comparison of thermally equivalent times (t_{43}) for the temperature profiles shown in Figure 6

To make use of the data in Figure 12, it is necessary to calculate the probability of an adverse biological effect for those **thermally equivalent times**. Limited data are available for this, but two cases are shown here. The first is for the most sensitive tissue shown in Table 1, i.e., the kidney. The threshold for necrosis of kidney glomeruli and tubules is approximately 20 min at 43 °C. Assuming a sigmoidal response, that the fraction of affected kidneys at the threshold is 5 %, and an extrapolation number n_e = 100, the calculated rate constant k = 0,175 s^{-1}. For the second example, the results for birth defects in mice [27] are re-analyzed, yielding n_e = 77 and k = 1,41 s^{-1}.

The calculated fractions of affected tissues or organisms are shown in Figure 13. A few points are worth mentioning. First, adult tissues show a range of responses to heat, see Table 1. This is also true of ionizing radiation. As noted above, the kidney is relatively sensitive to thermal exposures. Curves like that for kidney necrosis in Figure 13 would shift to the right for other tissues. Second, the **thermally equivalent time** needed to induce a birth defect is only about a tenth of that required to damage the soft tissue of the kidney [21], [27]. Third, the result for birth defects is based on data obtained with whole-body maternal heating. The relevance to the physically more confined exposures of diagnostic ultrasound is not clear. Fourth, these effects are rather severe, resulting in death of the tissue involved or malformation of the young organism. More subtle effects may need lesser doses than those illustrated here. Fifth, for many effects in tissues or organs, the range of **thermally equivalent time** over which the fraction affected increases from zero to >0,9 is about a factor of only 3.

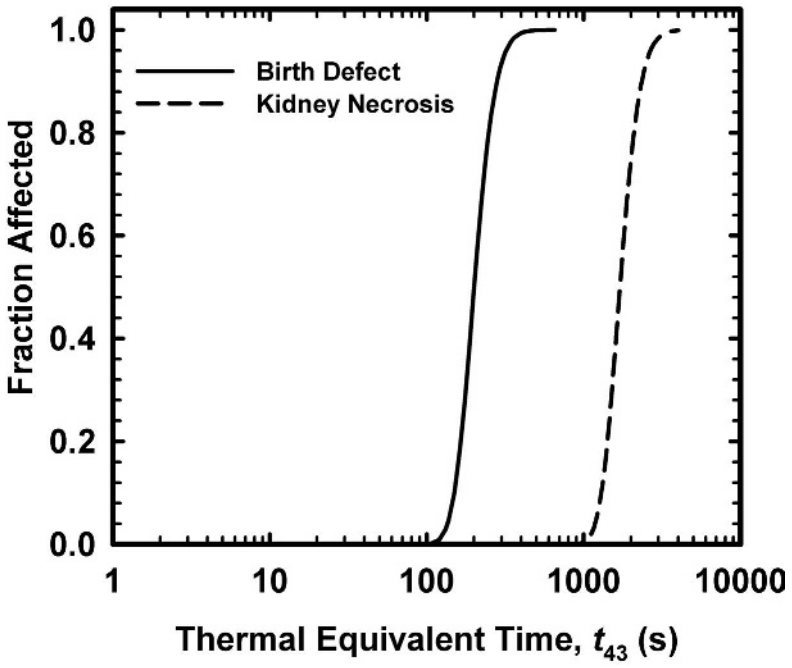
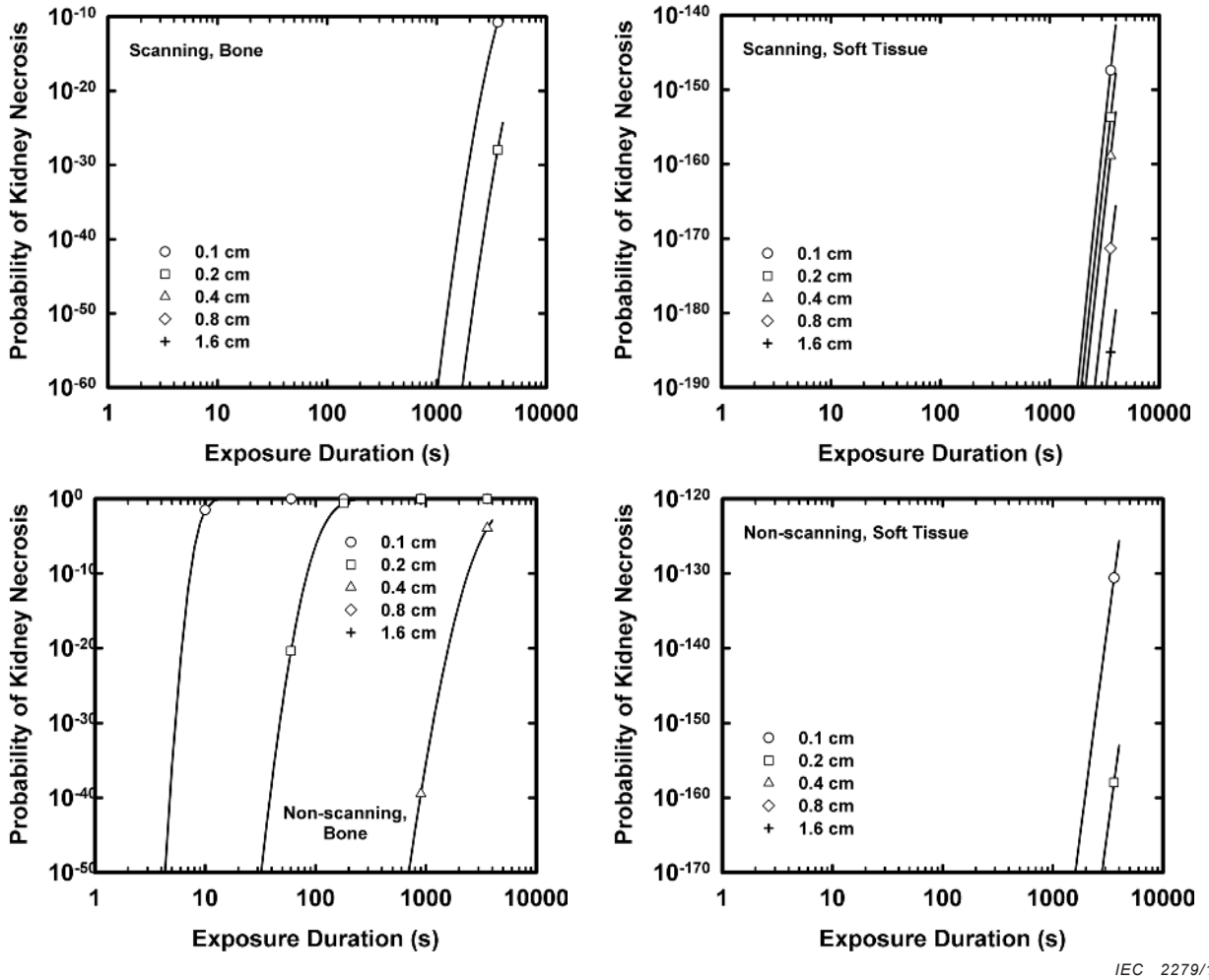


Figure 13 – Probability of birth defect or kidney necrosis as a function of thermally equivalent time (t_{43})

The calculated probabilities of kidney necrosis or birth defect are shown in Figures 14 and 15, respectively. The likelihood of kidney necrosis is usually quite small, the only exception being near bone for a non-scanning beam. The probabilities for birth defect are greater than for kidney in all cases, as would be expected from Figure 13. Imaging during the first trimester, i.e., before significant ossification has occurred, apparently entails a low probability of harm due to thermal exposure unless the duration of imaging is unusually long or the output is significantly greater than is assumed here. Imaging during the second or third trimester must necessarily expose soft tissue near bone, and the probability of injury with a non-scanning beam may become unacceptably great after only a few seconds. The exposure durations needed to produce similar probabilities of harm for scanned beams are up to two orders of magnitude larger than for non-scanning beams for small beam widths, but this difference disappears for widths above 0,8 cm.



The relations were derived for five beam diameters in four models.

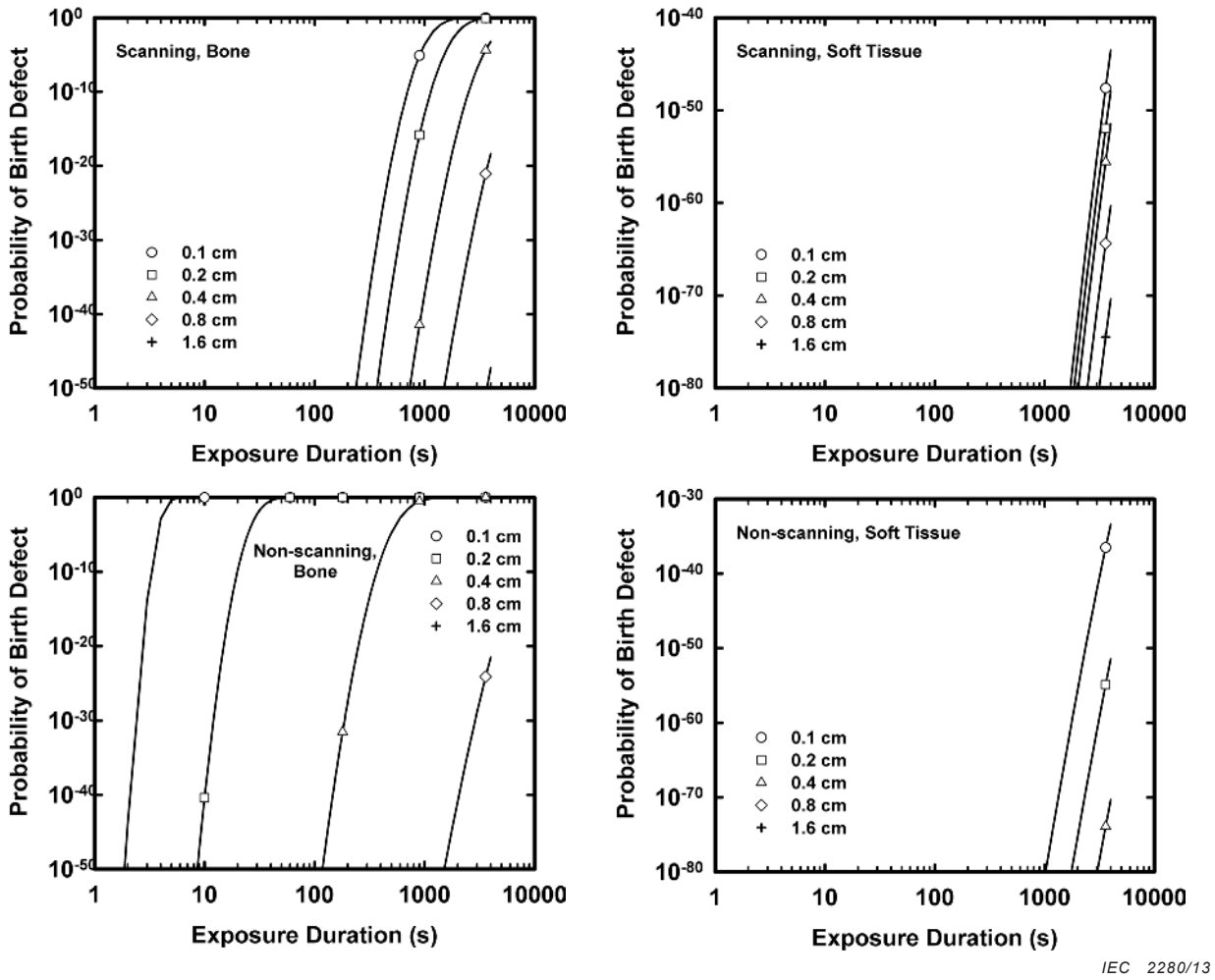
Figure 14 – Probabilities of kidney necrosis estimated for the thermally equivalent times (t_{43}) shown in Figure 12

To make use of these results for an onscreen safety display, it would be necessary to choose an upper limit on the risk to the patient that one was willing to accept, determine the **thermally equivalent time** at that level, calculate a curve such as those in Figures 15 or 16 for the heating produced by the acoustic field generated by the transducer of interest, and determine the corresponding exposure duration required to attain that **thermally equivalent time**. The value of **thermally equivalent time displayed** to the user would be that exposure duration.

5.6.3 Advantages of the *TETD*

Replacement of the *TI* with the *TETD* offers the following advantages:

- The value displayed onscreen would be dimensional, having units of time. It would therefore be extremely simple for the user to interpret and implement in real time. The user would simply be told that it is potentially dangerous to continuously scan the same tissue for a time greater than *TETD*.



The relations were derived for five beam diameters in four models.

Figure 15 – Probabilities of birth defect estimated for the thermally equivalent times (t_{43}) shown in Figure 12

- The use of *TETD* permits the use of higher output levels, at least for short imaging durations. Higher powers often improve image quality, particularly for deep tissues imaged in harmonic mode and for Doppler techniques.
- The *TETD* offers a more direct indication of risk to the patient. If the duration of imaging is less than *TETD*, and assuming that the same tissue has not been scanned multiple times in a short period, then it may be concluded that the risk to the patient is at least very small, possibly nonexistent.
- The displayed value of *TETD* is based on a direct assessment of the probability of harm to the subject. It is therefore associated in a fundamental way with the process of risk management advocated by the IEC. Under the *TETD*, the process of risk assessment moves from a rather subjective exercise to become a more objective, mathematically tractable problem; error analysis also becomes quantitative.

5.6.4 Shortcomings of the *TETD*

Replacement of the *TI* with the *TETD* is subject to the following limitations:

- The *TETD* and *TI* share the same basic model for tissue heating. Thus both parameters have the same problems in attempting to estimate *in vivo* temperature elevations from average, or worst-case, values for important physical factors such as **acoustic absorption** and **attenuation coefficients**, insertion loss, thermal conductivity, heat capacity and perfusion length.

- Nonlinear propagation may occur when the acoustic path contains a significant amount of fluid or other low-attenuation material. The effect increases with output, and because TI_{cur} assumes linear propagation, this can introduce significant error into the calculation for intensity [3]. Technical specification IEC 61949 provides a method for minimizing these finite-amplitude effects when they occur during the calibration procedures for diagnostic transducers and suggests a method for estimating *in situ* exposure. However, use of this method is not currently required when making measurements of the physical quantities needed to determine the TI-value.
- Depending on its method of implementation, the $TETD$ may provide an estimate of risk at a location that does not coincide with the region of interest, an effect that may be of particular concern when the foetus is involved.
- There are few well-researched curves relating thermal exposure to the probability of an effect. Further, most experimental data have been collected for exposures leading to intentional hyperthermia for cancer therapy. Extrapolation to lower temperature rises or shorter exposure durations, or both, may be problematic.
- The $TETD$ is a new concept. It will require considerable effort to demonstrate that its underlying model is applicable to the ultrasonic fields generated by actual clinical transducers. As part of the needed studies, it will be desirable to consider the optimal method for implementing the **thermally equivalent time** as a real-time display.

6 Summary

The various significant characteristics listed as “Advantages” or “Shortcomings” for the three approaches discussed above are summarized in Table 6. The purpose of the table is to allow easy comparison among the possible modifications to the TI, thereby facilitating discussion and selection of the optimal revision. In general, the wording of some of the attributes has been intentionally adapted to allow a “Yes” to be interpreted as favourable, and “No” as unfavourable, to its selection.

Table 6 – Comparison of significant characteristics of the possible replacements for the TI.

Property – Display	TI_{new}	$TETI$	TT	SUT	$TETD$
Reflects the probability of an adverse event	Yes	Yes	Yes	Yes	Yes
Implies high outputs should be avoided (if possible)	Yes	Yes	Yes	Yes	Yes
Incorporates a convenient reference to current TI	Yes	No	No	No	No
Value is dimensional	No	No	Yes	Yes	Yes
Value is easily interpreted	Yes	Yes	Yes	Yes	Yes
Property – Method					
Could be implemented quickly	Yes	Yes	No	No	No
Can accept lower-quality exposure-response data	Yes	Yes	No	No	No
Incorporates the thermally equivalent time	Yes	Yes	No	No	Yes
Incorporates the time course of the temperature rise	No	No	Yes	No	Yes
Permits higher outputs (for short times)	No	Yes	Yes	Yes	Yes
Quantifies the duration of “safe” imaging	No	Yes	Yes	Yes	Yes
Concentrates on shorter exposures	No	No	Yes	Yes	No
Incorporates the concept of a threshold for an effect	No	No	Yes	Yes	No
Insensitive to values chosen for physical parameters	No	No	No	No	No
Insensitive to nonlinear propagation	No	No	No	No	No
Always estimates risk for the region of interest	No	No	No	No	No

7 Recommendations

7.1 General

This clause contains recommendations for topics that may be addressed initially within IEC TC87, with possible future inclusion by IEC SC62B in the IEC 60601 series standards.

7.2 Thermally equivalent time index

The implementation of the new index *TETI* should be investigated because it provides an easily understood number that more accurately quantifies the thermal risk from exposure to diagnostic ultrasound. To accomplish this goal, it is recommended that a Technical Specification be written to allow use of the *TETI* in selected imaging modes and/or techniques that require long dwell times, i.e., long exposures of the same region of interest. If implementation of the *TETI* is found to be both practical by manufacturers and desirable for sonographers, a new International Standard can then be written. Implementation of the potential new standard would be incorporated in a future revision of IEC 62359. For this new index to be adopted by SC62B in IEC 60601-2-37, some change to the normative sections of that standard may be necessary, but changes to one or more informative annexes certainly would be needed. In addition, it would be prudent to notify entities implementing that standard of the contemplated change.

7.3 Other models

Additional research should be carried out into *TT*, *SUT* and *TETD* with a view to implementing one of these in the future. Fortunately, the three approaches are sufficiently similar that much of that effort will be applicable to all. The topics to be addressed include:

a) improved methods for estimating the **temperature rise** *in situ*;

b) verification that these methods reflect the **temperature rises** produced by diagnostic transducers;

c) for *TT* and *SUT*, determination of generally accepted **threshold temperature rises** for induction of one or more biological effects of concern;

d) for *TETD*, determination of generally accepted exposure-response curves for induction of one or more biological effects of concern.

Following the successful outcome of the research projects listed above, a decision regarding implementation of *TT*, *SUT* or *TETD* should be made. Because *TT*, *SUT* and *TETD* are dimensional quantities rather than nondimensional indices, implementation of the selected approach would require extensive revision to both IEC 62359 and, if adopted by SC62B, IEC 60601-2-37. The necessary changes would involve the rationale behind the approach, the mathematical formulation and the informative appendices describing the use of the new display.

Bibliography

Standards publications

IEC 60854, *Methods of measuring the performance of ultrasonic pulse-echo diagnostic equipment*

IEC/TS 61949:2007*. Ultrasonics – Field characterization – In situ exposure estimation in finite-amplitude ultrasonic beams*

Other publications

[1] AIUM/NEMA (American Institute for Ultrasound in Medicine/National Electrical Manufacturers Association). *Standard for Real Time Display of Thermal and Mechanical Indices of Diagnostic Ultrasound Equipment. American Institute of Ultrasound in Medicine*, Laurel, MD; 1992.

[2] NCRP. *Exposure Criteria for Medical Diagnostic Ultrasound. I. Criteria Based on Thermal Mechanisms*. NCRP Report No. 113. Bethesda, MD: National Council on Radiation Protection and Measurements, 1992.

[3] NCRP. *Exposure Criteria for Medical Diagnostic Ultrasound. II. Criteria Based on All Known Mechanisms*. NCRP Report No. 140. Bethesda, MD: National Council on Radiation Protection and Measurements, 2002.

[4] WFUMB (World Federation for Ultrasound in Medicine and Biology). WFUMB symposium on safety of ultrasound in medicine, Kloster-Banz, Germany 1996. *Ultrasound Med Biol* 1998; 24(Suppl 1).

[5] ABRAMOWICZ, JS, BARNETT, S, DUCK, F, EDMONDS, P, HYNYNEN, K, ZISKIN, M. Fetal Thermal Effects of Diagnostic Ultrasound. *J Ultrasound Med,* 2008;27:541-559.

[6] O'BRIEN, WD Jr, DENG, CX, HARRIS, GR, HERMAN, BA, MERRITT, CR, SANGHVI, N, THOMENIUS, KE, ZACHARY, JF. The Risk of Exposure to Diagnostic Ultrasound in Postnatal Subjects – Thermal Effects. *J Ultrasound Med* 2008; 27:517-535.

[7] ABBOTT, JG. Rationale and derivation of MI and TI – A review. *Ultrasound Med Biol* 1999; 25:431-441.

[8] LUBBERS, J, HEKKENBERG, RT, BEZEMER, RA. Time to threshold (*TT*), a safety parameter for heating by diagnostic ultrasound. *Ultrasound Med Biol,* 2003; 29:755-764.

[9] AIUM/NEMA (American Institute for Ultrasound in Medicine/National Electrical Manufacturers Association). *Medical Ultrasound Safety*. American Institute of Ultrasound in Medicine, Laurel, MD; 1994.

[10] DUCK, FA. *Physical properties of tissue: A comprehensive reference book*. London (UK): Academic Press, 1990.

[11] HEKKENBERG, RT, BEZEMER, RA. *Aspects concerning the measurement of surface temperature of ultrasonic diagnostic transducers*, PG/TG/01.246r, ISBN 90-5412-078-9, March 2002.

[12] HEKKENBERG, RT, BEZEMER, RA. *Aspects concerning the measurement of surface temperature of ultrasonic diagnostic transducers, Part 2: on a human and artificial tissue*, PG/TG/2003.134, ISBN 90-5412-085-1, May 2003.

[13] HEKKENBERG, RT, BEZEMER, RA. On the development of a method to measure the surface temperature of ultrasonic diagnostic transducers. *Journal of Physics* Conference Series 1 (2004) 84-89 (Institute of Physics Publishing), 2004.

[14] CHURCH, CC. A Proposal to Clarify the Relationship Between the Thermal Index and the Corresponding Risk to the Patient. *Ultrasound Med Biol,* 2007; 33:1489-1494.

[15] ZISKIN, M. The thermal dose index. *J Ultrasound Med,* 2010; 29:1475-1479.

[16] KARAGOZ, I, KARTAL, MK. A new safety parameter for diagnostic ultrasound thermal bioeffects: Safe use time. *J Acoust Soc Am,* 2009; 125:3601-3610.

[17] EDWARDS, MJ, SAUNDERS, RD, SHIOTA, K. Effects of heat on embryos and foetuses. *Int J Hyperthermia,* 2003; *19:295-324.*

[18] MILLER, MW, ZISKIN, M. Biological Consequences of Hyperthermia. *Ultrasound Med Biol,* 1989; 15:707-722.

[19] DEWEY, WC, HOPWOOD, LE, SAPARETO, SA, GERWECK, LE. Cellular responses to combinations of hyperthermia and radiation. *Radiology,* 1977; 123:463-474.

[20] SAPARETO, SA, DEWEY, WC. Thermal dose determination in cancer therapy. *Intl J Radiation Oncology,* 1984; 10:787-800.

[21] DEWEY, WC. Arrhenius relationships from the molecule and cell to the clinic. *Int J Hyperthermia*, 1994; 10:457-483.

[22] MILLER, MW, NYBORG, WL, DEWEY, WC, EDWARDS, MJ, ABRAMOWICZ, JS, BRAYMAN, AA. Hyperthermic teratogenicity, thermal dose and diagnostic ultrasound during pregnancy: implications of new standards on tissue heating. *Intl J Hyperthermia,* 2002; 18:361-384.

[23] GLASSTONE, S, LAIDLER, KJ, EYRING, H. *The Theory of Rate Processes*. New York, USA: McGraw-Hill Book Co., Inc., 1941.

[24] JOHNSON, FA, EYRING, H, POLISSAR, MJ. *The Kinetic Basis of Molecular Biology*. New York, USA: John Wiley and Sons, Inc., 1954.

[25] CARSTENSEN, EL, MILLER, MW, LINKE, CA. Biological effects of ultrasound. *J Biol Phys,* 1974; 2:173-192.

[26] KIMMEL, GL, CUFF, JM, KIMMEL, CA, HEREDIA, DJ, TUDOR, N, SILVERMAN, PM, et al. Skeletal development following heat exposure in the rat. *Teratology,* 1993; 47:229-242.

[27] SHIOTA, K. Induction of Neural Tube Defects and Skeletal Malformations in Mice following Brief Hyperthermia in utero. *Bio. Neonate*,1988; 53:86-97.

[28] CHURCH, CC, MILLER, MW. Quantification of risk from fetal exposure to diagnostic ultrasound, *Prog Biophys Mol Biol,* 2007; 93:331-353.

[29] EDWARDS, MJ. Congenital defects in guinea pigs: fetal resorptions, abortions and malformations following induced hyperthermia during early gestation. *Teratology,* 1969; 2:313–328.

[30] EDWARDS, MJ. Congenital defects in guinea pigs: prenatal retardation of brain growth of guinea pigs following hyperthermia during gestation. *Teratology,* 1969; 2:329–336.

[31] NYBORG, WL. Solutions of the bio-heat transfer equation. *Phys Med Biol,* 1988; 33:785-792.

[32] PRESTON RC, SHAW A. *Measurement good practice guide. Recommended ultrasound field safety classification for medical diagnostic devices*. NPL Report No. 50. Teddington, UK: National Physical Laboratory, 2001.

[33] GEFAU. *Ultrasound field safety classification for medical diagnostic devices*. Duisburg, Germany: Gesellschaft für angewandte Ultraschallforschung, 2001.

[34] Minister of Public Works and Government Services (Canada). *Guidelines for the safe use of diagnostic ultrasound*. Publication 01-HECS-255. Ottawa, Canada, 2001.

[35] O'BRIEN, WD Jr, YANG, Y, SIMPSON, DG. Evaluation of unscanned-mode soft-tissue thermal index for rectangular sources and proposed new indices. *Ultrasound Med Biol,* 2004; 30:965-972.

[36] CHURCH CC. Thermal Dose and the Probability of Adverse Effects from HIFU, *Proceedings of the 6th International Symposium on Therapeutic Ultrasound*, Coussios CC, ter Haar G, eds. AIP Report No. 911, Melville, NY: American Institute of Physics, pp 131-137, 2007.

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