Safety of ultrasonic examinations; thermal and mechanical indices

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Abstract

This review article combines the reports on the biophysical effects in ultrasonography and provides the rationale behind the mechanical index (MI) and thermal index (TI) complying with the Output Display Standard (ODS). Safe ultrasonic doses are determined according to specific rules, and the screen displays the associated quantities MI and TI. The introduced indices MI and TI take into account the physical mechanism of interaction between ultrasounds and biological tissue, which depends on the temporal and spatial parameters of the acoustic field generated by ultrasound transducers. The predicted temperature increase is determined using three different tissue models: homogeneous, layered and bone/tissue interface.

Keywords: ultrasonography; thermal index; mechanical index; cavitation; International Electrotechnical Commission standards

Introduction

Based on current available experimental studies, there is a generally accepted view that diagnostic use of ultrasound is completely harmless to humans. Unfortunately, the current state of knowledge does not give us a categorical answer to this question whether there really are no side effects associated with the propagation of ultrasound in tissues.

The literature on the subject confirms the fact of empirical treatment of the mechanisms of ultrasound impact on living organisms. Experimental data only allows to assess the lowest ultrasound intensities at which no biological effects were observed.

In clinical applications, the results obtained are a compromise between image quality and depth of examination. The deeper the organs are, the greater the acoustic power should be used. The selection of permissible ultrasonic power is made taking into account the minimization of biological effects. In the USA, the acceptable ultrasound doses are regulated by guidelines developed by the Food and Drug Administration Center for Devices and Radiological Health (FDA), while in Europe by the International Electrotechnical Commission (IEC). Current full information on the acoustic values of the output parameters together with information regarding the adopted intensity levels can be found in numerous publications [1-8].

In the frequency range from 0.5 MHz to over 20 MHz, no harmful effects of ultrasound were found for intensity, peak in space and averaged over time, $I_{\text{SPTA}} < 100 \text{ mW/cm}^2$ and for sonication times $t$, for which the product of $I_{\text{SPTA}} \cdot t$ is less than 50 J/cm² [9].

Frequency is one of the main parameters affecting the resolution of ultrasound imaging systems. However, as the attenuation of the acoustic wave in tissues increases with the increase in frequency, the use of high frequency transducers for imaging structures at greater depths requires an increase in acoustic power, while with the same output power, lower frequency transducers should be used.

Acoustic intensity has a decisive influence on penetration depth. We usually specify two values of ultrasound intensity (or power); total intensity on the trans-
The purpose of this review is to provide a general overview of the rationales behind the biophysical mechanisms of cavitation and heating, monitored using MI and TI indices. Three different thermal indices are discussed: Soft-tissue Thermal Index (TIS), Bone Thermal Index (TIB) and Cranial-bone Thermal Index (TIC). A brief review of the safety of the recent ultrasound imaging technologies such as ultrafast imaging, vector Doppler, ARFI, and shear wave elastography is also given.

**Physical mechanism of ultrasound interaction on biological tissue**

In 1992, North American Manufactures Association (NEMA) and American Institute of Ultrasound in Medicine (AIUM) adopted the same method for standardizing ultrasonic diagnostic equipment and placing relevant information on the screen of the device based on Output Display Standard (ODS) [2,3].

There are two basic mechanisms, thermal and non-thermal, of interaction of ultrasound on biological tissues [9-12]. Usually both effects occur simultaneously, but with different intensity. The exception is lithotripsy, where mechanical effects are actually the only mechanism that destroys kidney stones [13].

The non-thermal mechanism involves cavitation and non-cavitational activities that are associated with certain mechanical aspects of the ultrasound field. They can be described as a function of such phenomena as radiation pressure, torque and acoustic flux (streaming) [14,15].

Acceptable intensities of ultrasounds are measured in water and then the calculations take into account the attenuation of the ultrasonic wave in the tissues along the path between the source and specific areas in the tissue. It is generally accepted that the average attenuation coefficient along the beam axis in the body is 0.3 dB/(cm•MHz).

The derated value of peak rarefractional is given by

$$P_r(z) = P_{0,r}(z) - \text{peak pressure amplitude reduced by } 0.3 \text{ dB/(cm•MHz)} \text{ to a point on the beam axis lying in tissues distant by } z \text{ cm from the ultrasonic transducer}$$

The international standard IEC 62359 (2nd edition) describes the ideas of ODS and explains in detail the rationales and derivation of equations describing thermal and mechanical phenomena in tissues [4].

Table I summarizes the output intensities of the apparatus in accordance with applicable standards.

### Table I. Limitations of acoustic outputs from diagnostic ultrasonic devices [3,4].

<table>
<thead>
<tr>
<th>Clinical application</th>
<th>Intensity ISPTA (mW/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>before the introduction of ODS</td>
<td>current level</td>
</tr>
<tr>
<td>Imaging of fetuses and newborns</td>
<td>94</td>
</tr>
<tr>
<td>Pediatrics and others</td>
<td>430</td>
</tr>
<tr>
<td>Cardiology/Peripheral vessels</td>
<td>720</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>17</td>
</tr>
</tbody>
</table>

ISPTA – Peak intensity in space and averaged over time, ODS – Output Display Standard
otic fluid [16]. The temperature increase is proportional to the pulse duty factor, i.e. to the quotient of the pulse duration and pulse repetition time [17,18].

There are at least two mechanisms for thermal loss – blood perfusion and heat conductivity. Blood perfusion is an effective factor in removing heat. The degree of blood perfusion varies depending on the type of tissue: the best perfused organs include the kidneys, heart and brain, while resting bones and muscles are the least perfused. The thermal conductivity is almost the same for all tissues and is similar to the conductivity for water, with the exception of bones, which have high conductivity and fat, which is less conductive compared to tissues [19].

**Cavitation mechanism**

Non-thermal effects are cavitational and non-cavitational [20]. The concept of cavitation refers to phenomena related to the vibrations and dynamics of movement of small gas bubbles present in the ultrasonic field [7,14]. At the first approximation, microbubble diameters of approximately 1 μm are assumed. Such bubbles can grow until their diameter increases to a size corresponding to the mechanical resonance of the bubble [21,22]. Near the resonance frequency, the vibration amplitude of the bubble wall is large and may be even 100 times larger than the displacement of the media for the beam at equilibrium [23]. If the bubble does not brake during sonication, we are dealing with stable cavitation as opposed to destructive cavitation, where the amplitude of wall vibrations is so high that the bubble collapses [24]. This implication generates a strong shock wave, which is accompanied by extremely high values of local temperature – up to 10,000 K [25]. In addition, the increase in temperature is accompanied by the implosion of free radicals such as hydroxide and hydrogen radicals. These radicals are very active and can cause undesirable biological effects, such as spontaneous biochemical reactions between tissues. Some tissues, e.g. lung tissues, may be more susceptible to phenomena such as cavitation compared to others.

The formation of cavitation bubbles has been repeatedly confirmed in lithotripsy [26-28]. In other therapeutic applications, the formation of microbubbles in tissue in vivo has not yet been documented.

An important effect of the mechanical action of ultrasound is the phenomenon of micro-acoustic flux generated by oscillating microbubbles. And although we do not observe the spontaneous formation of cavitation bubbles, the effect of microstreaming has been confirmed in the vicinity of microbubbles injected into the vascular system in the form of contrast agents. Microstreaming is also a major factor in changing membrane permeability.

In order for the new ODS standards to make sense, it is necessary to understand on what basis the indices, thermal TI and mechanical MI, were introduced.

The reason for introducing these indicators is the fact that the intensity value alone does not give an accurate assessment of the sonication of biological structures. Other factors, such as a rise in temperature or the possibility of mechanical vibration of tissues, may carry information about tissue changes or damage. The increase in temperature and the possibility of cavitation, in turn, depend on factors such as total output energy, shape of the ultrasonic beam, focus position, center frequency of the ultrasonic pulse and the Frame Rate (FR).

The displayed TI values give valuable information about the way in which the selected imaging mode settings, in particular the focus position setting and the scanning pulse amplitude (and therefore the MI value) affect the average ultrasonic wave intensity and power, and thus allow assessing the potential risk of mechanical and thermal effects on scanned tissues [29].

**TI Thermal Index**

TI values determine approximate levels of temperature rise in tissues exposed to ultrasound waves of given parameters. Due to the difficulties of modeling thermal phenomena associated with various types of interaction of ultrasonic energy with the human body, simplified models based on averaged conditions were introduced [13].

In the soft tissue model, homogenous absorption along the pulse propagation path is assumed and the coefficient of attenuation is equal \( \alpha(f) = 0.3 \text{ dB/(cm}\cdot\text{MHz}) \). In the bone thermal model, very high ultrasound absorption in the surface layer of the bone is assumed, \( \alpha(f) \approx 15 \text{ dB/(cm}\cdot\text{MHz}) \).

Three different categories of TI indices (TIS, TIB, TIC) have been defined, corresponding to different combinations of anatomical structure of soft tissues and bones that are found during imaging [30].

Generally, the thermal index TI is defined by the relationship [3,4],

\[
TI = \frac{W_p}{W_{deg}} \quad (1)
\]

where \( W_p \) is the acoustic output power for selected test conditions and depth of interest, \( W_{deg} \) is the estimated power needed to increase the tissue temperature by 1°C, calculated on the basis of the selected thermal model.

It is assumed that the estimated acoustic power in milliwatts necessary to increase the soft tissue temperature by 1°C is for soft tissue

\[
W_{deg} = \frac{210[mW \cdot MHz]}{f[MHz]} \quad (2)
\]
The acoustic power necessary to raise the temperature by 1 °C in bone is much lower, since the absorption of ultrasound in the bones is much higher compared to that in soft tissue, and is assumed to be equal for uniform beam for bone $W_{beam} = 40\text{[mW/cm]} \cdot d\text{[cm]}$ (3) where $d$ is the ultrasonic beam diameter in centimeters at the selected depth.

The Soft-tissue Thermal Index (TIS) provides information about the temperature increase inside soft, homogeneous tissues, which is the case in abdominal examinations where only soft tissues occur.

When imaging in B mode, the tissue thermal model is used, and is assumed to have the highest temperature in cellular activity as a function of temperature. It was shown that biological effects depend not only on the local elevation in temperature, but also on the exposure time [34,35]. The estimate of time describing the thermal exposure is referred to as thermal dose $t_{REF}$ defined as [36,37],

$$t_{REF} = t \cdot R^{(T_{REF} - T)} \quad (8).$$

For humans $t_{REF}$ was defined as 43° [35,38] and R is fixed at R=0.25 for $T<43 \text{°C}$ [34,38]. For fetal studies $t_{REF}$ was assumed to be $t_{REF}=1$, and after rearranging eq. (8) the empirical formula specifying the maximum time for sonication of an organ without harmful thermal tissue effects has the form [34],

$$t \text{ (seconds)} = 43^{T - T_{REF}} \quad (9)$$

where $T$ is the temperature in degrees Celsius.

The relationship between sonication time and temperature rise is plotted in figure 1.

For example, an increase of 1 °C gives a time of 625 minutes, an increase of 2 °C limits the time to 256 minutes, while the theoretical increase of 6 °C to a critical level of 43 °C limits the examination time to 1 minute.

The potential risk of causing thermal effects in particularly sensitive organs during fetal scanning increases regardless of whether the beam is scanned or not being scanned. The TIC is equal,

$$TIC = \frac{W_0 \text{[mW]}}{d \text{[cm]} \cdot 40 \text{[mW/cm]}} \quad (7)$$

where $W_0$ is the total output power in milliwatts radiated by the transducer, $d$ is the transducer aperture.

In eye scanning applications, it is recommended that TIS is monitored and its value should be limited to a maximum of 1.0 [32,33].

Thermal indices are relative indicators of a possible rise in temperature at an interesting point along the propagation axis of the ultrasonic beam. The reason for using the term “relative” is that the mechanism of tissue heating is so complicated that the assumed index cannot determine the actual temperature rise for all possible conditions. Thus, a TI of 2 means higher temperature increases than a TI of 1, but does not necessarily mean a 2 °C increase. The TI must not exceed a value of 6 for short sonication times. Recommended exposure time and TI values are addressed in BMUS Guidelines [33]. In General abdominal and Peripheral vascular application “short time” (BMUS Guidelines [33], page 9) is given as 5 seconds for $5.0 < TI \leq 6.0$. Limiting TI to maximum value of 6 is also addressed in few papers [4,29,31,33].

Concerns about the increase in temperature caused by ultrasound in the body are based on the observed changes in cellular activity as a function of temperature. For example, an increase of 1 °C gives a time of 625 minutes, an increase of 2 °C limits the time to 256 minutes, while the theoretical increase of 6 °C to a critical level of 43 °C limits the examination time to 1 minute.

The potential risk of causing thermal effects in particularly sensitive organs during fetal scanning increases...
linearly with exposure time, but exponentially with temperature. The risk associated with heating also strongly depends on the time and speed of the scan and the presence of bones in the examined area. Thermal indices reach maximum values in the spectral Doppler and color Doppler modes, especially in vascular and cardiac studies [39].

**MI Mechanical Index**

The Mechanical Index MI was introduced to assess possible mechanical effects. Examples of mechanical effects relate to movement (or streaming) around compressible gas bubbles under the influence of ultrasonic wave pressure passing through the tissues and cavitation related energy causing cracking of the gas bubbles.

In lithotripsy, mechanical bioeffects can be caused by ultrasound waves with the same peak pressure as ultrasound sometimes used for diagnostic imaging, although in a completely different frequency range, below 1 MHz [40]. The center frequency of one complete cycle of the focused pulse from lithotripsy equipment is in the range 0.1 to 1 MHz. Spatial-peak temporal-peak positive and negative pressures can exceed 50 MPa and -10 MPa, respectively.

The probability of their occurrence increases with increasing peak pressure, but decreases with increasing ultrasound frequency. It has been shown that there is a threshold value below which the effect will not occur until a certain initial level is exceeded [7,41].

Although the existing limited experimental data suggest a linear frequency relationship, a more conservative root-frequency relationship was eventually selected [7].

The mechanical index is now defined as:

$$MI = \frac{\rho_{r, a}}{\sqrt{f_{av}} \cdot C_{MI}} \quad (10)$$

where $C_{MI} = 1\text{MPa} \cdot \text{MHz}^{-1/2}$, $\rho_{r, a}$ is the rarefractional pressure (in MPa) of the acoustic field derated at 0.3 dB (MHz cm)$^{-1}$ (after replacing decibels with Nepers the rarefractional pressure is equal $\rho_{r, a} = P_{r, a} \cdot 10^{-0.015 \cdot f_{av} \cdot z}$, $P_{r, a}$ is the maximum derated value of peak rarefractional or negative pressure amplitude in MPa, $z$ is the distance in centimeters from the transducer to the selected depth, $f_{av}$ is the acoustic-working frequency in MHz.

Equation (10) is based on a homogeneous tissue model and a derating factor which is a compromise. Other attenuation models were evaluated and rejected, such as fixed distance models [8] and the use of a homogeneous tissue model with a higher attenuation factor value more representative of many radiological and cardiac imaging applications. However, using more than one attenuation model would entail an increase in equipment complexity and need for user input to select appropriate attenuation schemes. Therefore, it was not felt that the extra complexity in attenuation modeling was justified given the level of understanding of the conditions required to produce mechanical bioeffects. With the selected compromise attenuation model, the mechanical index is simple to implement, use and, most importantly, sufficient to allow users to minimize acoustic output and any corresponding potential mechanical bioeffects.

The MI gives a relative indication of the potential for mechanical effects, such as cavitation (the violent collapse of a bubble in tissue), which in scanning modes may be more significant than thermal effects. According to the Output Display Standard [3,17] the MI can range up to 1.9 for all uses except ophthalmic, which has a maximum MI limit of 0.23.

The introduction of MI and TI indices has created favorable conditions for safer use of modern ultrasound scanners. Based on the available literature, we can formulate general advices that will help in a safe, daily diagnostic ultrasound examination:

1. Ultrasound imaging can only be used by trained medical personnel with the required permissions
2. Medical stuff performing ultrasonography should follow current reports on the safety of ultrasound examinations.
3. At the beginning of the examination a low level of emitted ultrasonic power should be set, and then modify (up or down) from this level until a satisfactory image or Doppler signal is obtained, keeping track of the TI or MI.
4. The duration of the examination, i.e. the organ’s exposure to ultrasonic waves should be as short as possible – it is a particularly important condition in prenatal examinations and eye imaging.
During the test, the values of TI and MI indices should be monitored, keeping them as low as possible, ensuring the correct imaging of the examined organ. In obstetric tests, in the first eight weeks of pregnancy, the TIS index is particularly important, while in the rest of pregnancy we control the TIB index.

In general, in obstetrics the examination should be as short as possible [36]: fetal heart rate should be measured rather using M-Mode; if a Doppler test is required, it can be carried out on devices that meet the international standards; factory default power setting in obstetric testing is TI <0.7; shorten the test if the TI exceeds 0.7 and MI <0.7 is recommended.

In obstetrics, during first trimester, pulse and color Doppler should not be used routinely; the examination should be as short as possible; pulse Doppler can be used when there are clinical indications, TI <1.0, no more than 5-10 minutes; examination of the mother’s uterine vessels safe when the fetus is outside the irradiated field.

For neonatal ultrasonography even for small MI ~ 0.3, there is a potential risk of lung damage – scanning should be as short as possible. For MI> 0.7 the risk of cavitation increases, especially in studies with contrast agents.

In transcranial studies in adults recommended TI is <1.0; do not exceed TI> 3.0; MI> 0.7, with extreme caution in the presence of contrast agents.

In table II are listed the exposure times and thermal indices recommended for various diagnostic applications.

New ultrasonic imaging modalities

Regulations and guidelines regarding thermal biological effects in ultrasonographic imaging assume equilibrium models of tissues in which the temperature rise is caused by a series of short ultrasonic impulses propagating in the tissues. In the last decade new imaging methods have been introduced, such as Acoustic Radiation Force Imaging (ARFI), Shear Wave Elastography (SWE), plane wave imaging and vector Doppler.

During the propagation through a soft tissue the ultrasonic pulses are absorbed and scattered/reflected. The wave loses energy and this process results in generation of volumetric radiation force acting in the direction of wave propagation. This phenomenon is used in new ultrasonic modalities of imaging the elastic properties of tissue.

In ARFI, the long (30-300 μs) “push” pulses generating the tissue displacement of 1 to 10 μm are used [42]. Similar push pulses are used in supersonic SWE imaging [43].

Despite much longer impulses than those used in standard ultrasound, no harmful biological effects accompanying the new imaging modalities have been demonstrated yet.

Nightingale et al [44] reported a very limited temperature rise ranging from 0.02 to 0.2 °C for individual excitation concluding, that less energy is required to displace tissue by several microns than to raise its temperature by a fraction of a degree Celsius. Similar findings of temperature increase from a single ARFI “push” on the order of 0.1°C in soft tissue were reported by Dall et al [45].

Hermon et al [46] showed relatively small, ~0.35 °C elevation of temperature in soft tissue for push pulse with intensity <720 mW/cm². However, at bone the temperature rise could even reach 8°C.

Hsu et al [47] stressed, that while in B-mode the highest temperature is near the transducer face, in ARFI and SWE modalities the largest greatest temperature elevation increase is at the focus.

Bruno et al [48] emphasized that acoustic energies are similar in ARFI modes (MI from 1.3 to 1.6) and in the standard gray scale ultrasonography. The thermal safety of ARFI has been experimentally confirmed with both in vitro measurements and finite-element method models [49]. Recently, in the review article Issaouia et al [50] analyzed the experimental and epidemiologic data from 25 articles and showed that SWE maintained the same thermal effect as pulsed Doppler ultrasound used in obstetrics. However, the effects of very short duration energy peaks of the radiation force focused ultrasound remain unknown and should be explored by further experimental studies.

In ECMUS safety aspects of the elastography report [51], two important conclusions are; when acoustic radiation force impulses are used, significant temperature

<table>
<thead>
<tr>
<th>Midwifery - general</th>
<th>Limit the test time if TI&gt; 0.7; TI&gt; 3.0 not recommended, MI &lt;0.3 recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midwifery – 1st trimester</td>
<td>TI &lt;1.0, Exposure time &lt;5-10 minutes</td>
</tr>
<tr>
<td>Newborns brain and spine</td>
<td>Limited test time if TI&gt; 0.7</td>
</tr>
<tr>
<td>Adults – transcranial studies</td>
<td>Limit the test time for TI&gt; 1.0</td>
</tr>
<tr>
<td>Adults – general (without eyes)</td>
<td>Limit testing time for TI&gt; 1.0, not recommended TI&gt; 6.0</td>
</tr>
<tr>
<td>Contrasting agents</td>
<td>MI &lt;0.7</td>
</tr>
<tr>
<td>Training and research</td>
<td>Time &lt;2x time in clinical trials</td>
</tr>
</tbody>
</table>
risers may occur, especially if bone lies in the beam, and when using ARFI, the temperature has its maximum at the focus, whereas in B-mode the maximum is close to the transducer.

Another new imaging technology is based on plane wave generation with no focusing on transmit. Urs et al [52] measured the acoustic intensity parameters for the conventional and plane- and wave techniques compared to FDA 510k ophthalmic safety limits [1]. Ophthalmic FDA limits are: $I_{SPPA.3} = 28 \, \text{W/cm}^2$, $I_{SPTA.3} = 17 \, \text{mW/cm}^2$ and $\text{MI} = 0.23$. Measured plane-wave Doppler intensity and mechanical index values were: $I_{SPPA.3} = 3.0 \, \text{W/cm}^2$, $I_{SPTA.3} = 7.0 \, \text{mW/cm}^2$ and $\text{MI} = 0.07$, all values well below FDA limits. The reported results clearly showed that plane wave imaging and especially plane wave Doppler Mode have significantly lower instantaneous and temporally averaged intensities and mechanical index than the conventionally focused mode.

Similar results are expected in vector Doppler mode that is primarily based on plane wave transmit.

Conclusions

If the scanning system allows obtaining TI or MI greater than 1, then both indices, from the value of 0.4 up to a maximum should be displayed, which will help the user apply the ALARA principle (As Low As Reasonably Achievable). For every new patient to be scanned, a prudent starting point would be to set the machine for the lowest index setting, which is just below 0.4 (except for ophthalmic use, where the index is always kept below 0.23) and then modify (up or down) from this level until a satisfactory image or Doppler signal is obtained, keeping track of the TI or MI. It is important to stress that exceeding the maximal levels of TI and MI do not indicate that a biological effect is actually happening, but only inform the user concerning the relative probability of a biological effect. This is the reason for learning to implement the ALARA principle, using the TI and MI values that are as small as possible, while keeping the quality of the scan as high as possible.

Conflict of interest: none

References

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