Biomedical Ultrasound Fundamentals of Imaging and Micromachined Transducers

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Lecture - 47

Hello, and welcome to the lecture on bio-effects and safety. In our previous discussion, we covered safety in ultrasound imaging, focusing on how ultrasound interacts with tissues to create thermal and mechanical bio-effects. Fortunately, over the past 50 to 70 years, ultrasound has maintained an excellent safety profile, thanks to a vigilant research community that has prioritized safety. Significant basic research on cavitation and thermal effects has enhanced our understanding of these bio-effects.

In this lecture, we will explore the output display standard, which provides users with a direct on-screen index related to thermal and mechanical bio-effects, thereby improving safety. Here's a brief history of the development of thermal and mechanical indices: until the early 1990s, regulations primarily limited the acoustic outputs of ultrasound scanners. This regulatory framework continues today, with the FDA stipulating that the spatial peak temporal average intensity should remain below 720 milliwatts per centimeter squared. For the eyes, which are sensitive and have limited heat diffusion, the ISPTA must be less than 50 milliwatts per centimeter squared.

While these metrics are useful, it's crucial to understand the relationship between bio-effects and acoustic parameters. Notably, effects can be frequency-dependent and may vary depending on the type of tissue involved, indicating that intensity alone may not provide a complete picture. This is where the thermal index and mechanical index come into play; they were devised to relate these parameters to bio-effects. The thermal index and mechanical index serve as regulatory indicators that help predict the likelihood of bio-effects during diagnostic ultrasound.

Together, these indices form the output display standard, developed by a committee of scientists with guidance from regulatory agencies in the late 1990s. It is essential to recognize that these are relative indices, not absolute parameters. However, their presence on the screen during an ultrasound examination allows for comparison and recording. If future research reveals that a particular ultrasound setting led to a specific bio-effect, we would have a record of the corresponding thermal index and cavitation index used at that time.

Now, let's delve into the thermal index in greater detail. The thermal index measures the potential for tissue heating during ultrasound imaging. Tissue heating can occur due to energy deposition, which can happen in two primary ways.

To begin with, let's consider the process of absorption. In our previous lecture, we discussed how ultrasound attenuates as it propagates through tissue, with the majority of this attenuation occurring due to the absorption of ultrasound. For the purpose of this discussion, we will assume that the absorbed ultrasound energy is primarily converted into heat. Additionally, conduction from heated transducer surfaces can also contribute to tissue heating. For instance, in high-intensity focused ultrasound (HIFU) therapy, a modality that uses high-intensity ultrasound to destroy tumors, the treatment duration can be relatively long, leading to transducer heating. As a result, patients undergoing this treatment may experience surface burns due to direct conduction of heat from the transducer to the surrounding tissue. Therefore, tissue heating is a significant mechanism that occurs not only through absorption deep within the body but also from the surface conduction.

The extent of tissue heating can vary based on the type and location of the tissue as well as the transducer being utilized. Now, let's discuss the definition of the thermal index. The thermal index is defined as the ratio of the acoustic power produced by the ultrasound transducer specifically, the time-averaged acoustic power to the power required to raise the temperature of the tissue by one degree Celsius. Mathematically, this can be represented as $TI = \frac{W_0}{W_{deg}}$, where W_0 is the average acoustic power of the transducer, and W_{deg} is the power needed to increase the tissue temperature by 1 degree Celsius.

But how do we determine the power required to raise the tissue temperature by 1 degree Celsius? This is achieved using models of tissue heating, which are also validated through experiments. The thermal index serves as a link between temperature-predicting algorithms and the measured acoustic output parameter W_0. As mentioned, W_0 is a system-dependent parameter that can be calibrated by the manufacturer, allowing for the calculation of the time-averaged acoustic power generated by the transducer. Conversely, W_{deg} varies depending on the type of tissue being examined. As a result, the thermal index is defined separately for various categories of tissues, specifically soft tissue, bone, and bone at the surface. Therefore, we have three thermal indices: TIS (thermal index for soft tissue), TIB (thermal index for bone), and TIC (thermal index for cranium or bone at the surface).

Let's now focus on the thermal index for soft tissue (TIS). Where do we typically expect the maximum temperature rise to occur? This generally happens near the surface of the transducer, where the effects of conduction become more significant. Soft tissue exhibits relatively low absorption, meaning that the behavior and extent of heating at the surface can vary based on factors such as the type of transducer in use, the F-number of the transducer, aperture size, and the

geometry of the transducer itself. For array transducers, the area of beam overlap is where the highest temperature rise is usually observed.

This phenomenon can be illustrated in a schematic representation. In this scenario, we are firing a beam, shifting it, and firing again, resulting in four beams with some overlap between consecutive firings. Notably, the area of overlap receives energy from two beams rather than one, which leads to a greater temperature rise in that specific region.

There are various methods for imaging, one of which is plane wave imaging, where all transducers are fired simultaneously. We will explore this in more detail later, but when all transducers are activated at once, the maximum heating typically occurs at the surface of the transducer or the skin area that is directly in contact with it. To summarize, in transducer arrays, the region of beam overlap will exhibit the highest temperature rise. In contrast, for imaging techniques without scanning such as plane wave imaging the entire surface area of the transducer becomes the hotspot, where the maximum temperature increase is expected.

Now, let's discuss the thermal index for bone, referred to as TIB. Bones are known for their high attenuation properties, with most of this attenuation resulting from absorption. This characteristic leads to significant hotspots for temperature elevation. In configurations similar to the previous discussion, when bone is present in the imaging region of interest, the highest temperature increase is expected not only in the overlapping areas of the beam near the transducer surface but also at the bone interface. This trend persists even when using non-scanning transducers.

In cases of plane wave imaging, where the transducer emits sound waves without scanning, the highest temperature rise will still occur near the bone-soft tissue interface. Now let’s explore the thermal index for bone at the surface, or the thermal index for the cranium, abbreviated as TIC. If the bone interface is near the surface of the transducer, this area will likely experience the highest temperature rise. This observation aligns with what we discussed earlier regarding the overlapping regions of the beam being hotspots for temperature elevation.

This pattern also holds for non-scanned imaging transducers. For example, in plane wave imaging, where all transducers are activated simultaneously, the highest temperature rise is still expected near the interface between the bone and the transducer.

Next, let's consider the limitations of the thermal index. While the thermal index is a valuable tool, it is not an absolute metric. The potential for heat-related bioeffects depends on numerous factors, many of which are not addressed by the thermal index. Since it is based on a simplified theoretical model, it does have its limitations. This model assumes a steady-state behavior and fails to capture the dynamics of temperature fluctuations during ultrasound exposure.

Additionally, the thermal index considers only a few standard tissue types such as bone, bone at the interface, and soft tissue while ignoring the diversity and inhomogeneity of tissue types in the

body. Furthermore, it provides a basic consideration for perfusion but lacks a comprehensive approach to it. Lastly, the model assumes uniform exposure of ultrasound across the tissue of interest, which may not reflect the complexities of real-world scenarios.

Local hotspots are often overlooked in this context. Having covered the thermal index, let's now turn our attention to mechanical bio-effects, which are regulated by the mechanical index (MI). The MI is a regulatory index that indicates a threshold below which inertial cavitation is unlikely to occur. It represents the probability of cavitation in a medium based on the transducer's frequency and the applied pressure.

The development of the mechanical index stemmed from scientific observations of cavitation using high-amplitude sources, such as lithotripters. Researchers also conducted experiments on cells and lower organisms, where cavitation-induced bio-effects were noted, including some non-fatal hemorrhages observed in mice. These findings heightened awareness among scientists regarding the potential for cavitation in the human body, leading to the establishment of the mechanical index as a result of collaborative efforts between scientists and regulatory agencies.

The nucleation of bubbles in tissue is influenced by the peak negative pressure. As mentioned in the previous lecture, bubbles can form during the low-pressure phase or the rarefaction phase of ultrasound. These bubbles interact with the ultrasound beam, leading to various bio-effects. Inertial cavitation is contingent on the peak negative pressure and exhibits threshold behavior. This peak negative pressure is also referred to as peak rarefactional pressure.

When the peak negative pressure crosses a certain threshold, inertial cavitation occurs. Until that threshold is reached, there are qualitative and quantitative differences in cavitation behavior. However, once the threshold is exceeded, strong inertial cavitation is observed. Inertial cavitation is frequency-dependent and occurs after surpassing a specific peak negative pressure threshold. With this understanding, Apfel and Holland authored a seminal paper from which the mechanical index was derived.

The mechanical index is calculated as the derated peak negative pressure, which represents the pressure at the location of interest. I'll elaborate on the concept of derating in the next slide. The mechanical index formula includes the peak negative pressure in megapascals in the numerator and the square root of the frequency in megahertz in the denominator. To make the mechanical index dimensionless, it is adjusted with relevant units, yielding a simple numerical value.

The term "mechanical index" derives from the relationship $\frac{P^2}{f}$. While the formula presents $\frac{P}{\sqrt{f}}$, it connects to the concept that $\frac{P^2}{f}$ is proportional to the mechanical work done on a bubble during the negative phase of the acoustic cycle, thus justifying the name.

Now, let's discuss derating. Determining the acoustic pressure in situ is typically challenging to achieve in vivo; therefore, these measurements are often conducted in a water tank within a calibration system. An approximate derating factor is then applied. For example, if we assume an attenuation coefficient of 0.3 dB per centimeter per megahertz, we can assess how much the ultrasound beam weakens due to attenuation relative to the pressure measured in water. By applying this derating factor, we can obtain a reliable approximation of the in situ acoustic pressure in vivo.

To calculate the mechanical index (MI), we divide the derated peak negative pressure by the square root of the frequency in megahertz. The derivation of the MI is based on several key assumptions, significantly contributed to by Apfel and Holland, and supported by experimental measurements. Firstly, the model assumes the presence of all sizes of cavitation nuclei, which lead to bubble growth and, through inertial cavitation, collapse due to the inertia of the surrounding fluid. This process involves an initial rapid growth of the bubbles, followed by an even sharper collapse, characteristic of inertial cavitation. Secondly, the derivation focuses on short pulses similar to those used in diagnostic ultrasound, where damped transducers are utilized to eliminate ringing and achieve a short spatial pulse length. The model is applicable for duty cycles lower than 1 percent and does not apply to continuous wave insonation. Additionally, it assumes that the temperature reached inside the bubble during collapse can be extremely high, estimated at around 5000 Kelvin, which is a reasonable assumption given the dynamics of bubble collapse. The model also assumes isothermal growth of the bubble, meaning it remains in equilibrium with the surrounding environment during growth, followed by a sudden adiabatic implosion when the bubble collapses. Furthermore, the host fluid is considered incompressible; since water is largely incompressible, tissue can also be regarded as such due to its primarily water composition. Gas diffusion is neglected over the timescale of the oscillations to simplify the model, which is another reasonable assumption. Lastly, the model assumes that the rarefactional part of the acoustic cycle occurs first during the pulse. It is crucial to note that proper use of the MI requires careful consideration of the clinical context, with a recommended limit for soft tissue set at 1.9. Staying below this threshold is important to minimize the probability of inertial cavitation.

For sensitive organs such as the eye, the mechanical index (MI) limit is set at only 0.23, while for the lungs, which contain numerous gaseous pockets, the MI limit is lower than 0.7 due to the higher probability of inertial cavitation. This contrasts with soft tissue, where the presence of cavitation nuclei is less certain. Additionally, in contrast-enhanced imaging, the MI is typically kept below 0.1 to prevent bubble disruption and mitigate the risk of bio-effects from polydispersed microbubbles. It's important to note that the MI was not designed to predict bio-effects arising from stable cavitation in the presence of contrast agents. Recently, the Holland group introduced a new metric called the cavitation index, although it has not yet been adopted by regulatory agencies. While there is some correlation between higher MI and increased bubble disruption, the

MI is not an appropriate metric for assessing contrast agent destruction. Furthermore, the derivation of MI assumes short pulses and low-duty cycles, making it unsuitable for long pulse durations or continuous wave ultrasound insonation. Caution should also be exercised when applying MI to studies involving low kilohertz frequencies. For example, reports involving 40 kHz or 100 kHz ultrasound claimed safety based on MI values below 1.9; however, since the MI was derived for megahertz ultrasound pulses, its behavior at kilohertz frequencies may differ significantly.

In summary, today's discussion centered on output display standards, emphasizing how these standards help sonographers utilize ultrasound while minimizing risks. We explored the formulation and limitations of the thermal index and delved into the theoretical basis of the mechanical index. While we did not derive the MI, we discussed its correct application. With that, I conclude this lecture and look forward to seeing you in the next one. Thank you.