History of the American Institute of Ultrasound in Medicine's Efforts to Keep Ultrasound Safe

Wesley L. Nyborg, PhD
Physics Department
University of Vermont
Burlington, Vermont USA

Among the factors that have contributed to the rapid growth in the medical use of diagnostic ultrasound (DUS), an important one is the reputation for safety that it enjoys. This reputation did not come about immediately, and it has not been maintained without effort. Instead, the reassurance that users and patients can feel about the safety of DUS comes from years of research into the conditions under which hazards can be avoided and application of the findings to guidelines for equipment manufacture and medical practice. Efforts of this kind that have been made by individuals in many countries as well as by national and international organizations have been reviewed recently. This article emphasizes, in particular, the contributions of the American Institute of Ultrasound in Medicine (AIUM) to these efforts; it is part of a series of articles on various topics prepared in celebration of the AIUM's 50th anniversary.

In the earliest days of the AIUM, its members were involved mostly with applications of ultrasound in physical therapy; at the 1957 AIUM meeting, only 1 of 35 papers dealt with the possibility of using ultrasound for diagnosis. Thus, it was well known in the formative years of the AIUM that exposure of a patient to ultrasound is capable of producing physiologic change. In a therapeutic application, the aim, of course, is to produce a change for the better. It was known, though, from research with laboratory animals, that harm can be produced by ultrasound under some conditions, for example, as described by Lehmann (Fig. 1). As diagnostic techniques improved, the use of DUS increased rapidly, and by the late 1960s, the AIUM was concerned primarily with DUS applications. As this occurred, it was recognized that technical advice should be provided for avoiding harm from the use of this new modality and for increasing its effectiveness. For these purposes, the AIUM established committees, including those leading to the present Bioeffects Committee and Technical Standards Committee. The Bioeffects Committee was asked to provide information to the membership on matters relating to the biological effects of ultrasound, especially when these matters relate to the safety of clinical ultrasound.

From time to time, the Bioeffects Committee produced consensus statements on important matters. The first of these (later to be modified) was included in communications from the committee in 1976 and, after some revision, in 1978. An excerpt from the 1978 form of the statement is shown in Figure 2; accompanying this was text specifying the intensity referred to as the spatial-peak temporal-average (SPTA) value. Also, it was warned that the statement was based on all seemingly reliable data (from animal experiments) available at the time, although such data for operating conditions

Abbreviations
AIUM, American Institute of Ultrasound in Medicine; DUS, diagnostic ultrasound; MI, mechanical index; NCRP, National Council for Radiation Protection and Measurements; SPTA, spatial-peak temporal-average; TI, thermal index
closely resembling those for DUS were only beginning to become available, and, in particular, that “Little research has been done with repeated short pulses such as would be most relevant to diagnostic ultrasound.” These warnings are now known to have been well founded.

The Bioeffects Committee initiated an activity, which it continues today, of evaluating research publications considered to be relevant to the safety of diagnostic ultrasound, noting, among other things, whether there were findings that required revision of existing statements. Bioeffects Committee reports were published regularly in the AIUM’s official journal. All reports that were published during the period from 1962 through 1982 were republished in a single volume, and those that appeared in the period from 1985 through 1991 were republished in another volume. Also, in later years, the committee published a series of reports based on conferences, in each of which the present status of knowledge was reviewed and a consensus was reached on conclusions and recommendations.

In the earliest days of DUS, little information was available to purchasers of equipment on characteristics of the ultrasound fields produced. The AIUM Bioeffects Committee and Technical Standards Committee combined efforts to encourage manufacturers to provide specifications on such acoustic quantities as the frequency, total (temporal-average) power, and various kinds of intensity, as well as a few electrical quantities. A Manufacturer’s Commendation Panel was created, with the responsibility of offering awards and special privileges at AIUM annual meetings to manufacturers who agreed to include the desired data in operating manuals. Figure 3 shows one of the first certificates that was awarded for this purpose. Examples of the data provided can be seen in 2 reports from the panel. After 1985, the US Food and Drug Administration (FDA) used the force of law to achieve the Manufacturer’s Commendation Panel’s objectives: it became a federal requirement that relevant acoustic data be included in operating manuals for DUS equipment marketed in the United States. The AIUM commendation procedure was then gradually discontinued.
When this acoustic information first became available, many users of DUS equipment were not prepared for it because training programs for medical personnel intending to specialize in DUS were not yet well developed. In response to this problem, the AIUM Bioeffects Committee prepared brochures and reports in which acoustic terms were defined and their relevance to safety concerns were explained. The first of these (Fig. 4) was a small brochure designed to give the reader a nontotalizing approach to the terminology needed for understanding the 1978 AIUM statement (Fig. 2). This simple brochure was widely read and was followed later by more comprehensive reports, which defined terminology, explained concepts, and presented further recommendations as they were adopted. Also, textbooks appeared, such as a popular book by Kremkau (Fig. 5).

As of 1976, commercial medical equipment had to satisfy requirements of a federal law according to which new devices offered for sale in the United States were to be substantially equivalent in safety and effectiveness to devices marketed for the same applications before May 28, 1976. Diagnostic ultrasound was initially placed in a category for which each new product must be tested in clinical trials before it is approved for marketing; such trials can be very expensive and can take many years. However, panels appointed by the FDA reviewed evidence on the biological effects of ultrasound (especially, the evidence on which the 1976 AIUM statement was based) together with data on acoustic outputs of existing commercial equipment (eg, as reported by Carson et al [photograph and personal history published earlier]) and concluded that clinical trials were not needed for DUS equipment. Instead, it was decided that a manufacturer proposing to sell a new DUS device should submit product specifications to the FDA in a 510(k) premarket notification, according to an approved standard. The standard that was accepted was developed in a committee chaired by O'Brien (Fig. 6) and composed of individuals from the FDA, the Technical Standards and Bioeffects committees of the AIUM, and the Ultrasound Committee of the National Electrical Manufacturers Association.

According to the resulting FDA document, the quantities to be reported included acoustic power and intensities; see a discussion by Stratmeyer (Fig. 7). In addition to values of these quantities measured in water, estimates were to be included of the intensities produced in an average patient; these estimated in vivo quantities (“derated” quantities) would be less than those measured in water because of attenuation in the tissue and would be calculated on the basis of simplifying assumptions. In a survey of DUS equipment, it was concluded that the maximal derated output SPTA intensity did not exceed 94 mW/cm² for equipment produced before 1976 for obstetric applications. Hence, 94 mW/cm² was chosen as the limiting value of the derated SPTA intensity for future equipment, in accordance with the 1976 federal mandate. (It may be noted that this is not very different from the value, 100 mW/cm², to which the 1976 AIUM statement [Fig. 2] referred.)

Figure 3. AIUM manufacturer’s commendation award presented to Advanced Diagnostic Research Corporation in 1980.
In the first AIUM conference dealing with safety considerations,\(^9\) the emphasis was on thermal mechanisms, and there was a sharing of information with the National Council for Radiation Protection and Measurements (NCRP). (One of the NCRP committees, Scientific Committee 66, had been considering thermal mechanisms for several years and later published a report on the subject.\(^{23}\) It was recognized that the 1978 AIUM statement (Fig. 2) was roughly consistent with a statement that there were no known bioeffects from exposures of animals in which the temperature elevation did not exceed 1°C and was based on experiments with relatively broad unfocused beams, which had been summarized in a report.\(^{24}\) A revised statement was arrived at by use of computations showing that, with a narrow focused beam in soft tissue, a much higher SPTA intensity could be used without producing a temperature rise exceeding 1°C. Specifically, the 1976 statement was replaced by a 1987 statement (Fig. 2). In the text accompanying the latter statement, it was explained that the intensity is the derated SPTA value and that the –6 dB beam width of the focused beam is to be either 4 wavelengths or 4 mm, whichever is smaller. The tissue was assumed to be soft tissue, such as liver or brain. It was recognized, in agreement with indications being developed by the NCRP, that if the ultrasound beam impinges on bone or other highly absorbing tissue, the above-mentioned statement will not apply because the temperature rise produced by a given intensity can then be much higher as shown, for example, in experiments by Carstensen et al.\(^{25}\) and Drewniak et al.\(^{26}\) (photographs and personal histories of Carstensen and Dunn published earlier).\(^1\)
By the late 1980s, it had become evident to investigators that, although it continued to be important to base safety guidelines for ultrasound partly on thermal considerations, nonthermal mechanisms also had to be taken into account. It had been found that damage (capillary bleeding) could be produced in the lung of a small mammal by exposing it to pulsed ultrasound with characteristics approaching those of DUS without producing an appreciable temperature rise, as shown, for example, by Child et al. 27 The mechanism is evidently mechanical, in the general category of cavitation (the lung interior being a cavity or an assemblage of cavities), but its detailed nature has yet to be determined. It was found, for exposures to a pulsed ultrasound field, that a quantity that is critical in determining whether lung damage occurs is the local value of acoustic intensity (or better, the corresponding acoustic pressure) during the pulse. This is in contrast to the governing field characteristic for thermal damage, which would usually be a time-averaged quantity. For pulse regimens used in diagnostic ultrasound, the duty factor might be 0.001, so the time-averaged intensity might be 1000 times less than the value during a pulse. For lung damage in small animals at frequencies of 2 to 3 MHz, the threshold pressure amplitude is in the neighborhood of 1 MPa, which corresponds to a (traveling wave equivalent) intensity during the pulse of about 33 W/cm². If the duty factor is 0.001, the time-averaged intensity is then about 33 mW/cm². This is lower than the values for the SPTA intensity cited in the 1976 and 1987 statements (Fig. 2) and therefore indicates that the latter may be invalid for bioeffects produced by pulsed exposures.

The last decade has seen considerable change in the standards applied to commercial diagnostic ultrasound equipment in the United States. Users of DUS became convinced that the quality of images and Doppler signals could sometimes be improved by use of higher intensities and pressure amplitudes than were allowed under existing regulatory limits. To avoid inadvertent use of levels that might cause harm to the patients, it was proposed that information be presented on the screen or other display that would inform the user of the extent to which the instrument settings used might produce conditions that are hazardous. To implement this proposal, the AIUM and the National Electrical Manufacturers Association jointly
produced an “output display standard” for “real-time” display of safety information on diagnostic ultrasound equipment. In the output display standard, 3 “thermal indices” and a “mechanical index (MI)” were defined. The thermal indices (soft tissue TIS, bone TIB, and cranial TIC) are nondimensional quantities, which provide estimates of the maximal temperature rise likely to occur in a patient during a diagnostic ultrasound examination under different conditions; they are based partially on theory that had been used by the NCRP in formulating a TI. The MI, also nondimensional, is an indication of the possibility that harm could occur by mechanical action and is based on theory for inertial cavitation by Apfel and Holland. The availability of the above-described standards and the urging of numerous groups led the FDA to change its guidance for marketing of diagnostic ultrasound equipment in the United States. Under the new guidance, several “tracks” were described, any of which manufacturers might follow in obtaining approval. In track 3, the new philosophy of regulation was introduced, in which restrictions on the acoustic output were relaxed for equipment provided with features for display of safety information (Fig. 8). As an important example, the upper limit on the derated SPTA intensity was raised from 94 to 720 mW/cm² for devices to be used in fetal imaging if equipped with capabilities for display of the TIs and MI relevant to the operating conditions.

Efforts are under way to increase understanding of the displayed information among users and awareness by users that they have increased responsibility for patient safety when using equipment approved under the new FDA rules. Thus, Abbott reviewed the process by which the TIs and MI were developed, and the AIUM issued a publication for informing users on their importance. In a conference convened by the AIUM, the accuracy of the MI was one of the topics discussed. Also, in its latest report, the NCRP emphasized the importance of the information displayed under track 3 requirements and urged continued efforts for improving it.

Topics of concern treated by recent conferences and reports include the potential for cavitation associated with the use of contrast agents and errors that can arise from nonlinear propagation phenomena, which occur when ultrasound fields of high amplitude are measured in water.

In conclusion, in the years since the AIUM was formed, there has been a tremendous advance in the practice of DUS and, at the same time, an increase in understanding of the possibilities for biological effects. It is now more feasible than before to know, for any given operating conditions, whether there is a possibility of harm from either thermal or nonthermal mechanisms. Whereas users of DUS equipment once had available to them little more than simple specifications of the frequency and, perhaps, electrical power, with little indication of how these related to safety, they can now be presented with standardized indices on-screen, which are designed to alert them to conditions under which undesired temperature elevation or cavitation activity may occur.

Although putting safety information at the fingertips of operators during applications of diagnostic ultrasound marks an important advance, there is much need for continued research and development so that the information can be as accurate and relevant as possible. This is especially important because technologic and medical advances continue to add new capabilities, some of which may be accompanied by increased risk. The required effort and investment are well worthwhile to ensure that diagnostic ultrasound maintains its enviable record for safety in diagnostic applications.

References

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