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International Society of Ultrasound in Obstetrics and Gynecology (ISUOG)

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on behalf of the Executive Board of the International Society of Ultrasound in Obstetrics and Gynecology

BACKGROUND

Diagnostic ultrasound has had an extraordinary impact in medicine, and in obstetrics and gynecology in particular, since its introduction into clinical practice more than 40 years ago. Its growth has been phenomenal, from simple static B-scanning to real-time, M-mode, spectral and color Doppler and, most recently, three-dimensional imaging. This is due, in part, to the lack of proven harmful bioeffects. Epidemiologic studies are scarce, however, and the fact that harmful effects have not yet been detected does not prove safety. The latest technical developments in this field (including the transvaginal approach) give the potential that tissues may be exposed to higher ultrasound energy levels than previously.

Among manufacturers, the trend has been towards increasing the power output of ultrasound devices. The Food and Drug Administration (FDA) in the United States of America has regulated this output to levels believed to produce only minimal bioeffects and certainly not those that could be harmful. In the USA, manufacturers now have the option to increase output to levels eight or 10 times higher than in the past, provided certain safety factors appear on the instruments' monitors (output display). It is thus now the user's responsibility to make educated decisions regarding relative risk of a particular modality, and to weigh up the risk/benefit ratio of the examination. Education is, thus, pivotal.

The output display indices

The acoustic parameters previously used (peak rarefaction pressure, power output, spatial peak temporal average intensity [ISPTA] and spatial peak pulse average intensity [ISPPA]) have the inherent weakness that they do not correspond to directly measurable or observable effects in the insonated tissue. This makes it difficult for the average user to interpret the actual level of exposure. The indices presently displayed are the three thermal indices (for soft tissues: TIS, for bone: TIB and for adult cranial exposure: TIC) and the mechanical index (MI). Thermal index is calculated using the acoustic power output and ISPTA, and MI depends on peak negative pressure. The TI and MI, however, also take into account the ultrasound scanner settings that are under the control of the user, such as sample size or depth in Doppler mode. The thermal index represents an attempt to estimate the temperature rise in the field. It is approximately proportional to the temperature increase in °C (e.g. a TI of 2 means that the maximum temperature increase that may result from the exposure at those scanner settings is 2 °C). The MI (defined as the ratio of maximal peak rarefactional pressure to the square root of the ultrasound frequency) indicates the risk of mechanically induced damage in the insonated tissue.

Potential bioeffects

Ultrasound-induced tissue effects have been reported in several species but not, to date, in humans. Effects seen depend, in part, on the presence of gas and may also be due to heating. Nonthermal mechanisms that may produce effects are acoustic streaming, radiation forces, cavitation, and possibly secondary release of free radicals. Whereas the preterm infant's lungs may be at some risk from mechanical effects, due to the presence of air and the relative thinness of the visceral pleura and alveolar septa, the fluid-filled fetal lung does not seem to be at such risk. Similarly, hemorrhagic lesions in the intestines are unlikely in the human fetus where no gas is present. In the preterm newborn, intestines may be more susceptible particularly if peristalsis is diminished and the amount of gas increased, as is found in necrotizing enterocolitis. Similarly, the introduction of gas-carrier ultrasound contrast agents is likely to lower significantly the cavitation threshold. This effect may continue long after injection.

Heat (generated by nonultrasound devices) has been shown to be teratogenic in many animal species. The threshold is difficult to define, but a rise of 4 °C above core for 5 min seems to represent that threshold. In terms of thermal effects of ultrasound, in laboratory conditions where the transducer and the target are immobile and where little heat dispersion occurs, the rise in temperature at the target may be of several °C. This represents the 'worst case scenario'. When performing a clinical study,

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movements of the examiner's hand, the patient, the fetus (in obstetrics), and heat dissipation by vascular cooling and other mechanisms render the possibility of extreme temperature rise very unlikely. Caution should be exercised, however, if the pregnant mother is febrile, since fetal temperature is physiologically 0.5 °C higher than maternal body temperature. If the mother is febrile, the fetal temperature may, even without ultrasound insonation, already be elevated. Care should be taken when there is very little ultrasound energy attenuation by the maternal abdominal wall, such as is found in first trimester scanning through a full maternal bladder or in transvaginal ultrasound. A further issue to consider is heating generated at the surface of the transducer, particularly when performing intracavitary examinations.

In addition, acoustic absorption coefficient in bone (adult or developing) is very high when compared to that of soft tissues. Actively dividing tissue is more susceptible than mature tissue to damage by any external agent. In the fetus bone mineralization begins at 10–12 weeks of gestation, after which time cranial bone is present. One therefore has to keep in mind the possibility of excessive heating occurring in adjacent, actively developing nervous tissue. This would be especially relevant when using Doppler applications.

To date, none of the reported harmful effects of ultrasound in the nonhuman fetus has been confirmed scientifically in the human. Fetal growth delay, speech impairment, learning disorders, hearing disability, congenital malformations, and cancer induction have been studied using epidemiologic methods without any correlation with antenatal exposure to ultrasound being found. The only potential demonstrable effect was a slight increase in nonright-handedness among male, but not female, infants. The significance, if any, of this finding is unclear.

ULTRASOUND MODES

These are B-mode, M-mode, Doppler mode (spectral, color and power), and three-dimensional imaging.

B-mode

This mode is probably the safest since acoustic outputs are low, with ISPTA values ranging between 15 and 30 mW/cm^2. Temperature rise is most likely to be minimal, particularly since, in this mode in general, no one volume is insonated for prolonged periods due to the scanned nature of the beam. The only caveat should be cases in which there is a maternal pyrexia of 40 °C or above.

M-mode

Median ISPTA values are 2–3 times higher than with B-mode, but acoustic power is usually much less and thus risks are probably no higher than for B-mode applications.

Doppler ultrasound

Spectral Doppler mode can use intensities (ISPTA) which exceed 1 W/cm^2. In spectral Doppler, the ultrasound beam is kept at a specific position for relatively prolonged periods of time while the tracings necessary for measurement are obtained. In addition to potential local heating, other physical phenomena may occur as a result of the pulse radiation stress (tissue or cell displacement) and acoustic streaming (fluid displacement). Color Doppler ISPTA values are usually somewhat lower, in the vicinity of 200–300 mW/cm^2. This is still at least 10 times higher than the median values for B-mode. In color Doppler, the beam is scanned through the chosen region of interest and no one volume of the tissue runs the risk of being exposed to high intensities for prolonged periods, although limiting the volume of the box, as for instance in examining the fetal heart, may increase that risk. The use of color Doppler before applying spectral Doppler will reduce the time of exposure to spectral Doppler. Power Doppler and color Doppler are to be considered as one and the same mode with regard to the safety questions.

Some manufacturers provide the capability of superimposing a Doppler color box and a spectral Doppler gate on a B-scan (nonfrozen) image ('triple mode'). The ultrasound intensity reaching the target should be considered. It seems probable that the resulting energy is not the sum of the three, although little data is available.

Three-dimensional ultrasound

Since most of the time for this technique is spent in image reconstruction by a computer, the ultrasonic exposure time is similar to that of the B-scan modality. In addition, multiple regions of interest are scanned over time to obtain the necessary data and therefore the risk of bioeffects is minimal (probably similar to regular B-scan imaging).

STATEMENTS

The thermal (TI) and the mechanical (MI) indices are not perfect indicators of the risks of thermal and nonthermal bioeffects, but currently they should be accepted as the most practical and understandable methods of estimating the potential for such risks.

B-mode and M-mode

Acoustic outputs are generally not high enough to produce deleterious effects. Their use therefore appears to be safe, for all stages of pregnancy.

Doppler ultrasound

Significant temperature increase may be generated by spectral Doppler mode, particularly in the vicinity of bone. This should not prevent use of this mode when clinically indicated, provided the user has adequate knowledge of the instrument's acoustic output, or has access to the relevant

thermal index. Caution is recommended when using color Doppler mode with a very small region of interest, since this mode produces the highest potential for bioeffects.

When ultrasound examination is clinically indicated, there is no reason to withhold the use of scanners that have received current FDA clearance in tissues which have no identifiable gas bodies. Since ultrasound contrast agents are mostly gas-carriers, the risk of induction and sustenance of inertial cavitation is higher in circumstances when these agents are employed.

Pregnancy

Based on evidence currently available, routine clinical scanning of every woman during pregnancy using real-time B-mode imaging is not contraindicated.

The risk of damage to the fetus by teratogenic agents is particularly great in the first trimester. One has to remember that heat is generated at the transducer surface when using the transvaginal approach. Spectral and color Doppler may produce high intensities and routine examination by this modality during the embryonic period is rarely indicated. In addition, because of high acoustic absorption by bone, the potential for heating adjacent tissues must also be kept in mind.

Exposure time and acoustic output should be kept to the lowest levels consistent with obtaining diagnostic information and limited to medically indicated procedures, rather than for purely entertainment purposes.

Education of ultrasound operators is of the utmost importance since the responsibility for the safe use of ultrasound devices is now shared between the users and the manufacturers, who should ensure the accuracy of the output display.