Current status of safety of diagnostic ultrasound

Diagnostic ultrasound is generally accepted as a safe procedure in the absence of plausible and confirmed evidence of adverse health effects. However, it is impossible to rule out the possibility of adverse effects, as the scientific database is incomplete and cannot keep pace with technological developments and the enthusiasm to adopt new clinical applications. While acoustic outputs from diagnostic devices have increased considerably in the past decade, there have been no human studies on possible health effects from such exposures. Users of modern sophisticated ultrasonographic equipment are responsible for risk/benefit assessment.

IS THERE REASON FOR CONCERN?

Two factors create interest in safety issues in perinatal applications of ultrasound: relaxation of Food and Drug Administration (FDA) intensity limits on obstetric examinations and absence of relevant safety data. While there may be no serious cause for concern for most applications, the prudent use of ultrasound is justified. Obstetric applications are particularly susceptible as rapidly dividing and differentiating embryonic and fetal tissue is sensitive to physical damage, and the result of any perturbation of cell differentiation can be substantial.

Technological developments have brought about improved diagnostic acuity accompanied by substantially increased levels of acoustic output. In the enthusiasm to find new applications, clinical studies have been published on spectral Doppler flow measurements of yolk sac in early first trimester, while the benefit or potential risk is not established. Use of pulsed Doppler is encouraged in uncomplicated first trimester pregnancy, although there are no data from human studies on which to conclude the application is without risk. On the other hand, misdiagnosis is a real risk to the patient, and there is a need to establish the clinical benefit, if any, of procedures such as Doppler flow embryo-sonography. Unregulated use of freely available and inexpensive equipment by non-accredited or inadequately trained individuals presents an increased risk of misdiagnosis and harm.

Ultrasound exposures from modern diagnostic devices can produce measurable and significant biological effects resulting from both thermal and non-thermal mechanisms (Barnett and Kossoff, 1998). The FDA upper limit on intensity has been relaxed for obstetric examinations (allowing almost eight times higher intensity to the embryo or fetus) on the basis that the user will be guided on thermal risk by the thermal index (TI). However, the TI is not regulated, only the Ispta (spatial average temporal peak intensity). This parameter is not affected by change in acoustic frequency, but the rate of acoustic absorption (and the resulting temperature rise in tissue) increases with increasing frequency.

Modern ultrasound equipment combines a range of frequencies in complex scan modes to increase diagnostic accuracy. Change to higher frequencies, while complying with FDA limit on intensity, can significantly increase the ultrasound-induced temperature in embryonic tissue. Meanwhile, some non-thermal bioeffects have also been reported at diagnostic intensities.

DIAGNOSTIC ULTRASOUND CAN HEAT TISSUES

The amount of ultrasound-induced heating in obstetrics correlates with gestational age and development of fetal bone. Diagnostic ultrasound produces a modest temperature increase in soft embryonic tissue. While heating is greater in late pregnancy, the ultrasound beam is small relative to the size of the fetus, and localized tissue bioeffects can be more difficult to detect.

Because pulsed spectral Doppler examinations apply a stationary beam of relatively high intensity, tissue is readily heated resulting in increases of around 4.5 °C in the brain of animal fetuses insonated in utero (Barnett, 2000). The World Federation for Ultrasound in Medicine and Biology (Barnett, 1998) cautions that significant temperature increase can be produced by pulsed Doppler exposures, particularly near to bone, and recommends that:

> **'A diagnostic exposure that elevates embryonic and fetal in situ temperature above 41ºC (4ºC above normal temperature) for 5 minutes or more should be considered potentially hazardous.'**

There is some evidence to suggest that ultrasound-induced bioeffects can be potentiated by modest increases in temperature (Angles et al, 1990). There may be an increased risk to febrile patients from hyperthermic damage, since their elevated core temperature would add to the ultrasound-induced heating of the embryo or fetus. In all ultrasound applications, thermally induced adverse effects can be avoided by minimizing TI and duration of exposure.

NON-THERMAL STRESSES

Acoustic inertial cavitation is a non-thermal phenomenon that involves collapse of bubbles in liquids in a sound field and the sudden release of energy that can be sufficiently intense to disrupt molecular bonds and produce chemically-reactive free radicals. These free radicals may interfere with DNA causing chromosomal damage. Although this effect has been reported in contrived laboratory studies, it has not been directly observed in patients or in animals exposed to diagnostic intensities.

Capillary bleeding has been repeatedly demonstrated in lungs of various animal species following exposure to diagnostic ultrasound. As the onset of cavitation can occur within a diagnostic pulse, these bioeffects have been observed after exposures as brief as 20 seconds (Raeman et al, 1996). The presence of tissue/gas boundary interface is essential for this cavitation-related interaction, and there is no evidence of tissue damage in the fetus where the lungs are not inflated. There is a risk of lung haemorrhage in the premature neonate during pulsed Doppler echocardiographic examinations, but the clinical implications of this are uncertain.

The use of gas-encapsulated echo-contrast materials to enhance sonographic imaging increases the probability of cavitation. Cavitation-related biological effects can be avoided by reducing the peak amplitude, or by using a low value mechanical index on equipment with an output display. The presence of contrast agents should be taken into account when considering the risk/benefit ratio of an ultrasound examination.

Radiation pressure causes acoustic streaming of fluid along the path of the ultrasound beam. The associated stresses may interact and/or disrupt fragile embryonic tissue elements. In the absence of experimental evidence, it is assumed that the modest streaming velocities involved may not affect embryonic integrity. However, the potential adverse effect of combined acoustic streaming and mildly elevated embryonic temperature during pulsed Doppler exposure in first trimester pregnancy is yet to be determined.

HUMAN STUDIES

While there is no convincing evidence of a causal relationship between ultrasound exposure and adverse health outcome, the scientific literature contains occasional reports that are difficult to explain. Perturbation of neuron migration in the second trimester can produce subtle neurophysiological effects suggested as a possible mechanism for a report of increased incidence of non-right-handedness (Salvesen, 2000) in boys who were exposed to diagnostic ultrasound while in the uterus. It is difficult to attribute a responsible ultrasound mechanism from brief clinical exposure to B-mode scanning at the low intensity levels that were used in these studies.

While it is comforting that there is no conclusive evidence of serious adverse health effects from prenatal ultrasound exposures, there are obvious limitations in the database. Epidemiological data are derived from ultrasound exposure levels considerably lower than those available from modern ultrasonographic equipment. There are no data from perinatal applications using spectral or colour flow Doppler, or from other modern ultrasonographic procedures such as harmonic imaging techniques and application of echo-contrast agents.

FIRST TRIMESTER APPLICATIONS

Developing embryos and fetuses are sensitive to insult by physical agents. Because of the low acoustic absorption properties of soft embryonic tissue in early first trimester, it is unlikely that thermally mediated effects are an important safety consideration, particularly when dwell time is minimized. Non-thermal stresses may become significant by themselves or in combination with mildly elevated temperature. However, there are scant bioeffects data from which to evaluate potential adverse effects of ultrasound exposure of the embryo and early fetus.

CONCLUSIONS

While diagnostic ultrasound has a good safety record, a cautious approach is justified, particularly in the use of Doppler ultrasound in first trimester pregnancy. Scientific data are incomplete, and there are no epidemiological data for exposures of the type applied in current perinatal applications. With continuing changes in technology and development of new applications, its continued use as a safe and effective modality can only be assured if used according to recognized guidelines and by using the lowest exposure necessary to provide essential diagnostic information. Its use for non-medical purposes is professionally inappropriate. **HM**

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KEY POINTS

- Diagnostic ultrasound has a good safety record compared with other imaging modalities.
- Modern ultrasound diagnostic equipment can produce quantifiable biological effects.
- Pulsed Doppler exposures can produce significant heating of the fetus.
- Clinical implications of non-thermal effects are not fully evaluated.
- Human studies do not give convincing evidence of adverse effects, but there are significant gaps in current knowledge.
- Echo-contrast agents increase the likelihood of acoustic cavitation and present increased risk in perinatal applications.