Diagnostic Ultrasound Safety

A summary of the technical report "Exposure Criteria for Medical Diagnostic Ultrasound: II. Criteria Based on all Known Mechanisms"

issued by the National Council on Radiation Protection and Measurements

Physicians have used ultrasound to make images of the inside of the human body for nearly half a century. Most infants now born in the United States were exposed to ultrasound before birth. And in Germany, Norway, Iceland and Austria, all pregnant women are screened with ultrasound. To date, researchers have not identified any adverse biological effects clearly caused by ultrasound, even while three million babies born each year have had ultrasound scans *in utero* (while in the womb). This is an enviable safety record.

However, the National Council on Radiation Protection and Measurements (NCRP) advocates continued study of ultrasound safety, improvements in the safety features of ultrasound systems and more safety education for ultrasound system operators. Because of the sheer numbers of people exposed to ultrasound, any possibility of a harmful effect must be investigated thoroughly. This summary is drawn from a report that reviews the studies of ultrasound safety to date, and makes recommendations for further research and for improving the safeguards designed to ensure that the benefits of ultrasound continue to outweigh any risks.

About the NCRP

The NCRP is a non-governmental, not-for-profit, public service organization of scientists who work with radiation of all types. Its mission is to formulate and widely disseminate information, guidance and recommendations on radiation protection and measurements, representing the consensus of leading scientific thinking. The Council considers both *ionizing radiation* (such as X-rays) and *non-ionizing radiation* (such as ultrasound or microwaves). Governmental, non-governmental and industry organizations use the NCRP's recommendations as the scientific basis of their radiation protection programs. The NCRP also works closely with various international bodies concerned with radiation protection. NCRP programs are funded mainly through contracts with federal agencies for specific projects, and by donations from scientific societies and corporations with interest in radiation issues. The NCRP has built a broad base of contributors to assure that no one group will unduly influence its activities.

What is Ultrasound?

Ultrasound is like audible sound, except at a very high frequency, which means that the pitch is so high that the sound is inaudible to human beings. In diagnostic ultrasound, also known as sonography, the physician or technician places the *transducer*, or ultrasound probe, in or on the patient's body. Pulsed ultrasound waves emitted by the transducer pass into the body and reflect off the boundaries between different types of body tissue. The transducer receives these reflections, or echoes. A computer then assembles the information from the reflected ultrasound waves into a picture on a video monitor. The frequency, density, focus and aperture of the ultrasound beam can vary. Higher frequencies produce more clarity but cannot penetrate as deeply into the body. Lower frequencies penetrate more deeply but produce lower resolution, or clarity.

Why Review Ultrasound Safety?

Despite the impressive safety record of ultrasound to date, the NCRP continues to review ultrasound safety because ultrasound is being used in new ways, for new uses, and more and more frequently. In 1991, the US government relaxed their regulations and began allowing the *intensity* (or *acoustic output*) level of ultrasound used to scan the *in utero* fetus to increase almost eight times over the level that had been allowed previously. It can take many years to plan, execute and analyze a scientific study of the effects of ultrasound on the human population, known as an *epidemiological* study. As a result, virtually all of the studies so far of *in utero* ultrasound exposure tracked babies exposed to the earlier, lower acoustic output levels, not the higher levels allowed since 1991. Thus, the NCRP concludes that "the comfort obtained from the absence to date of any harm based on epidemiological evidence must be tempered by the fact that there are no epidemiological studies appropriate and adequate for current clinical practice."

If ultrasound exposure were causing a dramatic or novel effect on fetuses, it would be relatively easy to identify the effect. However, it is difficult, from a statistical point of view, to identify a slight increase in a common trait. And it is also difficult to pin down the cause of such a slight increase in a common trait. It is even more difficult, and a more lengthy process, when the trait is one that does not become apparent until years after birth. Another limitation of many studies on ultrasound exposure is that they have not always recorded exactly when in the pregnancy the fetus was exposed, or the type (the intensity, power, duration, frequency) of ultrasound that was used.

While it remains unclear whether there are any long-term effects of the diagnostic ultrasound in use today, scientists do know from laboratory studies that ultrasound at high intensities does create immediate effects at the time of exposure. From studies in test tubes, animals, and human beings, we know that ultrasound causes heating, referred to as ultrasound's *thermal* effect. Ultrasound also creates *nonthermal* effects, also known as *mechanical* effects. These nonthermal effects include audible sounds, the movement of cells in liquid, electrical changes in cell membranes, shrinking and expansion of bubbles in liquid, and pressure changes. Researching these thermal and nonthermal effects in the laboratory should help scientists to determine which long-term effects to check for in the human population.

Heat Effects of Ultrasound

When pregnant laboratory animals are exposed to hot baths, there is an increase in birth defects in their offspring. Pregnant women are warned not to go into hot tubs or saunas, even though the evidence of harm is less clear in human studies. It is not certain exactly how much heat is risky, and the risk would depend on how long the exposure lasts, and what stage of development the fetus is in. The most conservative estimates are that the temperature of the fetus should not safely rise more than 0.5 degrees Celsius above its normal temperature. It is also important to be aware that sometime in the last trimester, the normal temperature of the fetus rises to 0.5 degrees Celsius more than the mother's temperature, and remains elevated until after birth.

Some diagnostic ultrasound machines are capable of causing temperature rises of six degrees Celsius at the spot on which they are focused, if left in one spot. Continuous movement of the ultrasound probe helps to guard against dangerous temperature elevation in any one spot. In one study on newborns, ultrasound caused a temperature increase of 1.3 degrees Celsius, and blood circulated through the infant brains more quickly.

When exposed to stressful heat, mammalian cells produce *heat-shock proteins*. Scientists believe that these proteins somehow help to protect the cells against damage from heat. However, ultrasound heats the tissues so quickly that the cells may not have time to produce these protective heat-shock proteins.

The NCRP recommends that ultrasound machine operators be particularly aware that risks may offset the benefits of ultrasound exposures to the fetus when the temperature rise at the focal point of the ultrasound beam is calculated to be more than 3 degrees Celsius for ten minutes or more. However, in clinical practice it would be unusual for ultrasound to raise the temperature of any part of the fetus significantly for 10 minutes or longer.

Mechanical Effects of Ultrasound

In addition to heat, scientists have begun to learn more about the various types of mechanical effects that ultrasound can have on the body. They divide these effects into two categories. The first category is called *acoustic cavitation*. Cavitation can occur when sound passes through an area that contains a cavity, such as a gas bubble or other air pocket. Some tissues, most notably adult lung and intestine, do contain air bubbles, and are therefore more vulnerable to these cavitation effects. The fetal lung and intestine do not contain obvious air bubbles, because the fetus does not breathe air yet—it gets oxygen from the mother's blood stream. However, researchers believe that tiny bubbles could potentially form in parts of the body other than the lung and intestine. More research is needed in this area.

In cavitation, the sound waves can cause the bubbles or air pockets to expand and contract rhythmically: in other words, to pulsate, or resonate. When they pulsate, the bubbles send secondary sound waves off in all directions. These secondary sound waves can actually improve ultrasound images because the secondary waves also reflect back to the transducer, and provide more information. Thus, doctors now sometimes inject artificial bubbles known as *contrast agents* into the body before taking ultrasound images, for instance, of the circulatory system. However, these contrast agents are not used to image the fetus.

If the bubbles contract towards the point of collapsing, they can build up very high temperatures and pressures for a few tens of nanoseconds. These high temperatures and high pressures can produce highly reactive chemicals called *free radicals*, and other potentially toxic compounds which, although considered unlikely, could theoretically cause genetic damage. The rapid contraction of bubbles in cavitation can also cause microjets of liquid which can damage cells. When diagnostic ultrasound is focused on the lung or intestine of laboratory animals, which contain gas bubbles, these cavitation effects can cause ruptures in very small blood vessels.

The NCRP's safety guidelines for diagnostic ultrasound are designed to try to prevent cavitation effects, because these effects can be damaging. Restrictions on the pressure amplitude of the ultrasound pulse, in combination with awareness of whether or not there are gas bubbles in the tissue being imaged, can help to prevent cavitation. Other factors such as the length of the pulse, and the density of the liquid, also influence whether or not *cavitation* occurs. And if there are gas bubbles, the number, size and location of the bubbles also contribute to the effect.

Ultrasound can also create other mechanical effects that do not require the presence of bubbles in order to occur. These effects include changes in pressure, force, *torque* (causing things to rotate) and *streaming* (stirring of the liquid). These changes, in turn, can cause audible sounds, electrical changes in cell membranes that make them more permeable to large molecules, movement and redistribution of cells in liquid, and cell damage.

When ultrasound passes through liquid, it causes a sort of stirring action called *acoustic streaming*. As the acoustic pressure of the ultrasound increases, the flow of liquid speeds up. This stirring action, in theory, could occur in fluid-filled parts of a patient's body, such as blood vessels, the bladder or amniotic sac. In experiments with animals, when streaming of the liquid comes near a solid object, shearing can occur, and this can damage platelets and lead to abnormal blood clotting (thrombosis). It is not clear to what extent this effect occurs in humans exposed to diagnostic ultrasound.

Some studies have linked ultrasound to increased movement of the fetus at the time of the scan. One theory to explain this is that the fetus moves because it actually hears sound caused by the pressure of the ultrasound beam on the bones of the fetal head. At present, there is no evidence that hearing sounds during the ultrasound scan causes any damage to the fetus.

Healing with Ultrasound

Even before ultrasound became a widespread diagnostic tool, doctors were using it as a therapeutic tool. The fact that ultrasound does have biological effects on the body is clear from its uses to promote healing and even to operate on human beings. Ultrasound speeds the healing of bone, although it is not clear why this occurs. And surgeons are using highly-focused ultrasound beams to operate on delicate areas such as the eyes. The focused beam heats up and selectively destroys a minute portion of the tissue. Studying the therapeutic effects of ultrasound could also yield clues to any possible harmful effects of diagnostic ultrasound.

Studies in the Human Population

Because of the vast exposure of the general population to diagnostic ultrasound, any question of the possibility of harmful effects becomes very important. This is especially true for exposures of the fetus to ultrasound. In 1991, the US Government's Food and Drug Administration (FDA) began allowing the intensity of ultrasound used to scan the fetus to increase to 7.7 times its previous value, if manufacturers agreed to build new output displays into the ultrasound systems. While scientists have conducted many studies to try to determine whether there were any effects of ultrasound on the fetus, virtually all of these studies are of people exposed to ultrasound before the output levels were allowed to increase.

Based on their concerns about the theoretical effects of ultrasound on the developing fetus, researchers have conducted epidemiological studies looking for associations between ultrasound exposure and various traits, particularly with problems in brain development, growth, and childhood cancers. Even when an increase in a particular trait is associated, or linked, with ultrasound exposure in an epidemiological study, that does not necessarily mean that ultrasound is the cause of the increase in the trait.

So far, there is published data on whether or not *in utero* ultrasound scans can be linked to any of these traits: low Apgar scores at birth, birth defects, speech or hearing disorders, diminished height or weight in childhood, birth defects, chromosomal abnormalities, childhood cancers, and developmental problems including learning disabilities. There is no conclusive evidence that any of these traits were caused by the *in utero* ultrasound exposure experienced by these children. However, there is evidence from some of these studies linking some of these traits to ultrasound exposure—evidence which needs further investigation in order to be sure that the more intense ultrasound used today could not be causing these effects.

Many of the epidemiological studies only tracked a small number of people, rendering their conclusions less powerful. One way to get a bigger picture in cases like this is to review a whole group of studies that track a particular trait, in order to increase the number of people under consideration. In one review of more than 100 studies on ultrasound exposure, scientists grouped the studies of each trait in order to try to get a clearer picture of which traits might be linked to ultrasound. Grouping the three studies that looked at whether children were right or left handed, they found slightly more left-handedness among boys exposed to ultrasound *in utero*. Grouping the four studies on childhood cancer, they found no association between cancer and *in utero* ultrasound exposure. Out of eleven studies that looked at birth weight, two studies found an association between *in utero* ultrasound exposure and a small reduction in birth weight. Low birth weight is linked with various health risks to the newborn. But another study actually associated ultrasound with an increase in birth weight.

Even when there appears to be an association between ultrasound and a trait such as low birth weight, this does not prove that ultrasound is causing the trait. In some of these studies, women may have had more ultrasound scans because they already knew or suspected that there was some type of a problem with the fetus, and so these babies may be more likely to have problems, independent of their exposure to ultrasound. For instance, if the fetus does not seem to be growing enough, the mother may get ultrasound scans to check on the health of the fetus. If these babies are then born with low birth weights, it may be from a growth problem that predated the ultrasound exposure, and not a result of the ultrasound exposure. In other words, a statistical link between ultrasound exposure and a particular trait does not prove that ultrasound is causing that trait: there could be what scientists call a *confounding variable*.

One of the largest studies to date of *in utero* ultrasound exposure followed over 15,000 women in Australia. There was no reported increase in birth defects. However, the study was not designed to study birth defects, but to show that ultrasound screening decreases the incidence of health problems in newborns. So while reassuring, most scientists would not find this study conclusive. Another large study was designed to show that ultrasound screening in Canada would help to prevent prematurity. In this study, 1,415 women received ultrasound scans at five different points in their pregnancies, between 18 and 38 weeks. The other group of 1,419 women received only one ultrasound scan at 18 weeks. In the course of the study, they found that the offspring of the group that received more ultrasound scans had slightly lower birth weights.

One study found that 72 children with delayed speech had a higher rate of *in utero* ultrasound exposure than 144 children who did not have speech delays. However, the study did not describe why these children had been exposed to ultrasound, or the intensity or duration of the exposure. It is possible that they had ultrasound scans because of some other problem that also caused the speech delay. Once again, the association between ultrasound and speech delay does not necessarily mean that the ultrasound is the cause of the speech delay. The cause may well have been some third factor. And other studies have shown no association between ultrasound and speech delay. Nevertheless, the authors of this study recommended caution in using prenatal ultrasound.

Reviewing all the studies of the human population published so far, there are individual studies that found associations between diagnostic ultrasound and low birth weight, dyslexia, and delayed speech development. However, the NCRP found that there is insufficient evidence, even in these cases, to conclude that diagnostic ultrasound is the cause of any of these adverse effects, or any adverse effects whatsoever.

The inability to find convincing proof of an effect does not preclude the possibility of it happening. Part of the challenge in determining the effects of ultrasound is that researchers cannot, ethically, conduct laboratory experiments on human beings. The NCRP recommends that scientists conduct more studies in laboratory animals in order to identify any specific, subtle harmful effects that might be caused by ultrasound, and might arise in humans. Then, epidemiologists may be able to design bigger and better studies which could be targeted specifically to reaffirm that ultrasound, as it is used today, is not having any such subtle, harmful effects on the human population.

Ultrasound Systems Estimate Risks

Diagnostic ultrasound systems now come with displays meant to warn the system operator when there may be a risk to the patient (or fetus) from the heat or mechanical effects caused by ultrasound. The system displays numbers that provide crude measures of the risk. The Thermal Index (TI) is an estimate of risk from heat, and the Mechanical Index (MI) is an estimate of risk from the nonthermal effects of ultrasound. Manufacturers began incorporating these displays into ultrasound systems in order to meet the US government’s 1991 new regulations allowing them to increase ultrasound system outputs. If they used the Index displays, they could increase outputs. When the MI is above 0.5 or the TI is above 1.0, the NCRP recommends that the risks of ultrasound be weighed against the benefits.

As ultrasound waves pass through the body, their energy is converted into heat—heat absorbed by the tissues of the body. In general, the more dense the tissue, the more heat is absorbed, as the ultrasound waves cannot pass through dense tissue as easily. So fluid does not heat up very much, soft tissues heat up somewhat more, and bone heats up the most. If the ultrasound waves are passing through soft tissues, as is the case when scanning a fetus in the first trimester, the Thermal Index is calculated one way, known as the Soft Tissue Thermal Index, or TIS. If the ultrasound is focused near bone inside the body, as is the case for a fetus in the second or third trimester, the Thermal Index is calculated another way, known as the Bone Thermal Index or TIB.

However, the physician or technician who is using the ultrasound system must interpret these numbers in order to weigh the risks against the benefits of getting a better ultrasound image. Getting a better image may mean assuming greater risks. And in some cases the system operator needs to take into account the way that the ultrasound waves pass through that particular patient. For instance, the calculation of risk may be affected by whether the patient is thin or obese, whether or not they have a full bladder, or whether or not there are gas bubbles in the scanned part of the body.

The NCRP recommends that this system of assessing risk be improved in a number of ways. Scientists should continue to refine the formulas used to calculate the TI and MI estimates. Manufacturers should design ultrasound systems to automatically minimize the acoustic power and pressure while still yielding the desired images. Independent laboratories should conduct spot-checks of ultrasound systems to ensure that the information supplied by manufacturers about the output of the system is correct. And ultrasound operators should receive more education in evaluating risks and benefits. This training should be part of the process of ultrasound laboratory accreditation.

During the past decade the diagnostic capabilities and applications of ultrasound have increased dramatically. Part of the improvement in diagnostic capability is due to the higher acoustic intensity allowed for ultrasound by the US government, starting in 1991. At the same time, scientific knowledge of the biological effects of ultrasound has expanded. The medical community recognizes that they are responsible for maintaining the excellent safety record of diagnostic ultrasound. It is up to ultrasound technicians and doctors to evaluate the risks and benefits of diagnostic ultrasound in each case. The recommendations in this report are designed to bring as much information as possible to the physicians and ultrasound technicians faced with making these decisions.

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