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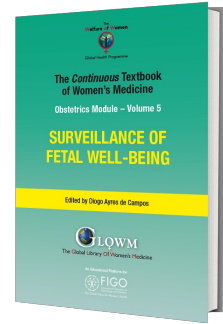
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### **SURVEILLANCE OF FETAL WELL-BEING**

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## *Chapter*

# **Effects of Ultrasound on Biological Tissues and Cells**

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## **INTRODUCTION**

Over the past five decades, ultrasound has become an essential tool in obstetrics, allowing the emergence of fetal medicine, and the resulting knowledge on fetal morphology, physiology and fetal-placental interaction. Obstetric ultrasound scans may use both transabdominal or transvaginal approaches, and sometimes take over one hour. Exposure to ultrasound occurs in virtually every pregnant woman in high-resource countries, and is an increasing reality all over the world.<sup>1</sup>

There are several benefits of ultrasound use in pregnancy, including accurate dating, determining implantation, viability, early diagnosis of multiple gestation, evaluation of fetal growth, detection of fetal anomalies, and abnormal placentation. However, the potential risks of any technology must not be disregarded, following the Hippocratic principle of *primum non nocere* (first do no harm).

Healthcare providers are sometimes questioned by pregnant women about the safety of ultrasound use. A vague answer is frequently given, such as “ultrasound is non-invasive and has been used for almost 50 years, so therefore it must be safe”. While there is a reasonable amount of truth in this answer, the concept of absolute safety does not exist, and there is a need to increase clinicians' knowledge on the potential biological effects of ultrasound.<sup>2</sup>

## **EVIDENCE ON THE BIOLOGICAL EFFECTS OF ULTRASOUND**

Ultrasound is a form of energy emission, a sound wave alternating positive and negative pressures, so it has the potential to produce biological effects on tissues and cells that cause harm to the fetus. There are two major mechanisms that may potentially affect embryonic and fetal tissues: thermal and mechanical.<sup>3</sup> Thermal effects result from the passage of ultrasound waveforms, with transformation of acoustic energy into heat. This constitutes the major potential adverse effect of obstetric ultrasound, with several reports existing of the deleterious effects of heat on embryos/fetuses in the animal model. These seem to occur when temperature rises 1.5°C above physiological levels.<sup>2</sup> Thermal effects depend on the type of tissue exposed, the duration of exposure, ultrasound mode, and the distance between tissue and emission source.<sup>4</sup>

Mechanical effects result from the alternating pressures that are generated.<sup>2</sup> The main effect occurs because of the interaction between ultrasound waves and gas bubbles present in tissues. Sound waves generate movement in and around gas bubbles, which can affect the surrounding tissues and lead to cavitation.<sup>4</sup> Ultrasonic cavitation causes mechanical damage, but it can also generate free radicals and other chemicals capable of damaging cell DNA.<sup>1</sup> Fortunately, this does not seem to be of great concern in obstetrical ultrasound, as the presence of air bubbles is necessary for cavitation to occur, and gas is nonexistent in fetal tissues, including lungs and bowel. It is unclear whether other non-thermal effects are of importance in obstetric ultrasound. Pulsed ultrasound can generate audible sounds that may possibly stimulate the fetus, and ultrasound beams have been shown to cause mechanical distortion of an elastic medium or fluid flow. The possible impact of such effects on the fetus is largely unknown.<sup>1</sup>

Some animal studies suggest that prolonged exposure to ultrasound waves can damage neurological, immunological, and hematological systems, as well as the genetic code of the fetus. Although biologic effects have been described in animal models, there is no evidence that these occur in humans. The World Health Organization (WHO) conducted a systematic review of the literature, and found no effects of obstetric ultrasound on the major adverse maternal and perinatal outcomes.<sup>5</sup> More specifically, exposure to obstetric ultrasound does not appear to increase the rate of low birth weight, preterm birth, low Apgar scores, need for neonatal resuscitation, seizures, admission to intensive care, neonatal, fetal or perinatal mortality. Growth and neurological development during infancy also seem to be unaffected. In particular, dyslexia, speech development, behavioral scores, school performance, reading and arithmetic scores, hearing, visual impairment and other neurological functions are unaltered. There is also no association with childhood malignancy, decreased adult intellectual performance, or mental disease. The authors of this review concluded that ultrasound use in pregnancy was not associated with any important adverse maternal, perinatal and childhood effect. The only effect that ultrasound may have on the fetus is the increased incidence of non-right handedness, although this seems to occur mainly in male fetuses and has minimal statistical significance.

Randomized controlled trials evaluating this topic have not been performed, and it is highly unlikely that these will occur, given the absence of effect seen in large observational studies and the almost universal use of ultrasound in modern obstetrics.

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## EVALUATING THE RISKS AND BENEFITS OF OBSTETRIC ULTRASOUND

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An evaluation of the risks of obstetric ultrasound can be approached in two distinct ways: the risk–benefit ratio and the precautionary principle. Clinicians are used to the risk–benefit principle, which is almost universally applied in medicine to justify diagnostic and therapeutic interventions. Use of a procedure will be justified if the benefits associated with it are judged to override the risks (recognized or presumed). This naturally assumes that the patient understands the risks and is willing to take them.<sup>2</sup> The precautionary principle is a more general concept, stating that if it is uncertain whether a procedure causes damage, the burden of proof regarding safety falls upon those advocating its use.<sup>6</sup>

There is strong evidence that the use of obstetric ultrasound does not carry increased risk of adverse outcomes (see above), but there is little information on safety regarding the duration of ultrasound exposure. Therefore, exposure to ultrasound should be limited to what is absolutely necessary, a rule that is also known as the ALARA principle (as low as reasonably achievable).

Non-medical use of obstetric ultrasound, for recreational purposes or for providing souvenirs to the family, is strongly discouraged.<sup>7</sup> These principles are clearly affirmed in the International Society of Ultrasound in Obstetrics and

Gynecology (ISUOG) joint statement on non-medical use of ultrasound: "There have been no reported incidents of human fetal harm in over 40 years of extensive use of medically indicated and supervised diagnostic ultrasound. Nevertheless, ultrasound involves exposure to a form of energy, so there is the potential to initiate biological effects. Some of these might, under certain circumstances, be detrimental to the developing fetus. Therefore, the uncontrolled use of ultrasound without medical benefit should be avoided. Furthermore, ultrasound should be employed only by health professionals who are trained and updated in clinical usage and bioeffects of ultrasound".<sup>8</sup>

Other potential risks of ultrasound are related to diagnostic errors, usually subdivided into overdiagnosis, underdiagnosis and erroneous reporting. These can lead to false reassurance, unnecessary follow-up or even termination of pregnancy. A description of these risks is beyond the scope of this chapter.

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## THE OUTPUT DISPLAY STANDARD (ODS)

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In 1992, the American Food and Drug Administration (FDA) agreed with ultrasound manufacturing companies to increase ultrasound power output, as higher outputs produce better images and consequently allow better diagnostic accuracy. As a consequence, output expressed by spatial peak temporal-average values increased almost 8-fold, changing from 94 to 720 mW/cm<sup>2</sup>.<sup>2</sup> In parallel, ultrasound manufacturers were asked to provide users with real-time quantitative safety-related information. The American Institute of Ultrasound in Medicine (AIUM), the FDA and the National Electrical Manufacturer's Association (NEMA) developed a standard, related to the potential thermal and mechanical bioeffects of ultrasound, known as the output display standard (ODS).<sup>9</sup>

Two types of indices are provided in the ODS: the thermal index (TI) indicating potential tissue temperature increases, and the mechanical index (MI) indicating the risks of this specific bioeffect. These indices are displayed on-screen in most modern ultrasound machines. TI is more important for obstetrics because, as stated above, mechanical effects are not expected in this setting. TI is the ratio between current total acoustic power, and the estimated acoustic power required to increase tissue temperature by 1°C.<sup>2</sup> A TI less than one is generally accepted as safe, because it is unlikely that the thermal increases of 1.5°C, associated with damage in animal studies, have been reached. However, it is important to remember that TI does not represent actual tissue temperature increases, but is no more than an estimation.<sup>10</sup> Similarly, MI is only an estimation of the cavitation potential of ultrasound.<sup>10</sup> As with TI, values less than one are considered safe.<sup>4</sup> In addition, TI has three variants: TIS for soft tissue, used mostly in early pregnancy when the degree of ossification is low; TIB for bones, used mainly in the second and third trimesters; and TIC for transcranial studies performed in the postnatal period.

TI and MI values usually remain low on routine first, second and third trimester ultrasound scans, as well as in Doppler studies.<sup>10</sup> ISUOG recommendations on the safe use of Doppler in the 11–13<sup>6</sup> weeks' scan state that pulsed Doppler (spectral, power and color flow imaging) should not be used routinely in this setting, but may be indicated in selected cases to refine the risk of aneuploidies. Exposure time should be as short as possible (usually no longer than 10 minutes and not exceeding 60 minutes). Scanning the uterine arteries in the first trimester is unlikely to have any biological effect on the fetus, as long as the latter is kept outside the Doppler ultrasound beam.<sup>11</sup>

The main purpose of developing the ODS was to help healthcare providers minimize potential hazardous effects of ultrasound. However, many healthcare providers using obstetric ultrasound are still unaware of their existence. In a questionnaire distributed to 145 doctors, 22 sonographers and 32 midwives from nine European countries, all of them using ultrasound on a daily or weekly basis, only one-third knew the meaning of MI or TI. Only 28% knew where to find these indices on the ultrasound machine, and only 22% knew how to adjust energy output. A similar survey conducted 8 years ago reached similar results.<sup>12</sup>

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## CONCLUSION

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Diagnostic ultrasound has been used in clinical practice for almost 50 years without any report of serious effects in human fetuses. However, biological effects causing tissue damage have been documented in animal models. Use of obstetric ultrasound in clinical practice should be guided by the principle of the lowest exposure time necessary, and use

for non-medical purposes should be strongly discouraged. Use of “output display standard” tools may provide additional reassurance that potentially deleterious effects of ultrasound are avoided.

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## PRACTICE RECOMMENDATIONS

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- **Although no deleterious effect of ultrasound has been reported in human fetuses, scans should use the lowest exposure time necessary.**
- **Ultrasound scans for non-medical purposes should be strongly discouraged.**
- **Healthcare providers who perform obstetric ultrasound examinations need to be aware of the output display standard (ODS), providing additional safety information.**

### CONFLICTS OF INTEREST

*The authors of this chapter declare that they have no interests that conflict with the contents of the chapter.*

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