Bioeffects and Safety of 2D and 3D/4D Ultrasound in Obstetrics—Is there a Place for "Parental Bonding" Scans?

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Abstract: Ultrasound is widely used in daily clinical obstetrical practice. Many medical indications exist for performing a sonographic examination but, in addition, several researchers have published information on the importance of patients watching the ultrasound monitor during the examination, particularly during three- and four-dimensional (3D/4D) scanning, for maternal-fetal bonding. Furthermore, a certain form of ultrasound, called "entertainment" or "keepsake" ultrasound has flourished, particularly in the United States. While ultrasound is assumed to be completely safe, it is a form of energy and, as such, has effects in tissues it traverses (= bioeffects). The two most important mechanisms for effects are thermal and non-thermal. Non-thermal mechanisms include cavitation, streaming, and even release of free radicals. These two major mechanisms are indicated on-screen by two indices: The thermal index (TI) and the mechanical index (MI). It is important to be aware of these effects to be able to prevent potential harm. Ultrasound machine controls can alter the instrument acoustic energy and hence the exposure but different machines behave differently. Therefore each clinician should know how this occurs in his/her own machine. Unfortunately, it appears the general knowledge in this area is poor and an effort should be made to educate the end-users. Whether 3D/4D enhances parental-fetal bonding is still a matter of discussion.

Keywords: Ultrasound, bioeffects, safety, maternal-fetal bonding.

INTRODUCTION

Ultrasound has become the most commonly utilized diagnostic imaging modality in obstetrics and gynecology. It is found in every academic department, both of Obstetrics/ Gynecology and Radiology, as well as in many private offices. In addition, stores are opening in malls over the USA, and, more recently in Europe, where pregnant patients can have an "entertainment" or "keepsake", non-medical ultrasound. The reasons for the extensive use of this modality are multiple: ultrasound is relatively easy to use (after appropriate training), results are immediately available, it is non-invasive and of relatively low cost when compared to other imaging modalities. Furthermore it has, so far, a perfect safety record. Besides some accepted clinical value in obstetrics, for instance adequate gestation dating and diagnosis of fetal abnormalities, it may have additional benefits such as increased bonding between future parents and their unborn child. Several modalities have been introduced in recent years: from spectral and color Doppler to three-dimensional/four-dimensional (3D/4D) ultrasound and ultrasound contrast agents. Several issues need to be addressed:

1. Can diagnostic ultrasound, as utilized in daily obstetrical clinical practice have effects on tissues and can these effects be harmful? This can be simply asked as: Is ultrasound safe for the fetus?
2. Is there any evidence that watching 3D/4D ultrasound on a monitor increases maternal-fetal (and, to some extent, paternal-fetal) bonding?

Bioeffects and Safety of Ultrasound in Obstetrics

Despite its widespread use, many scientists have expressed concern about the potential risks to the fetus. This began in the early days of diagnostic ultrasound,[1,2] has continued over the years,[3-17] with many cautioning against indiscriminate ultrasound exposure, as could, nowadays, entertainment ultrasound be considered. Ultrasound is a form of energy and, as such, has effects in tissues it traverses, i.e. biological effects, also called bioeffects.[18] The two major ones are local heating, the thermal effect, and tissue reaction to alternating positive and negative pressure, the non-thermal effect (also called mechanical) which includes effects that are not purely mechanical, such as chemical or physical.[19] It is important to consider what has happened over the years to acoustic outputs of clinical machines. In the United States, the original maximal outputs for different clinical applications date from 1985.[20] The spatial peak temporal average intensity ($I_{SPTA,}$ in mW/cm^2) was set at 17, 94, 430 and 720 mW/cm,[2] respectively, for ophthalmic, obstetrics, cardiac and peripheral vascular applications. Around 1991, there was a remarkable change in the regulations regarding

allowable upper limits of diagnostic ultrasound acoustic output levels to be 720mW/cm^2 for all applications (including obstetrical, i.e. an increase of a factor of almost 8) *except* Ophthalmic, which was set at 50 mW/cm.[2,21] This was in response to requests by end-users for improved diagnostic capabilities, thought to be obtainable by increasing the power output of the machines. However, it was recognized that there was increased potential for ultrasound-induced deleterious effects with an increased acoustic outputs. Therefore the FDA required these newer, more powerful instruments to provide the diagnostician with some indication of the potential for the occurrence of the two major recognized ultrasound-induced bioeffects: Thermal and non-thermal. Manufacturers were required to display on-screen the Thermal and the Mechanical indexes, TI and MI, respectively.[21, 22] There are 3 TI indices: for soft tissue (TIS), mostly used in the first trimester, for bone (TIB), used when the ultrasound beam impinges on bone, as in the 2nd and 3rd trimesters and for cranial scanning (TIC), mostly for adult scanning. It should be noted that time of exposure is not a factor in either index calculation. The concern in obstetrics is mainly for the risk of inducing a temperature increase. It is known that embryos are very sensitive to thermal insult.[23] There is a major debate in the literature whether there is a threshold below which risk does not exist[24] or if any positive temperature differential for any period of time has some effect.[25] It should be clearly understood that the TI is not an indication of actual temperature change.[26] It represents the ratio of the power of the machine at any given time to the power needed to raise the temperature by 1° C. Some imprecision exist, for example, a factor of 2 in the calculation algorithm, and thus, for example, with an on-screen indication of TI = 1, and considering just this aspect of imprecision (i.e. a factor of 2), the actual ultrasound-induced temperature at the target could be 1 ^{o}C, or it could be within the range of 0.5 to 2.0 ^{o}C. Furthermore, these indices are mathematical calculations based on certain models which may not always be identical to the clinical situation, for instance long fluid path as in polyhydramnios or surface heating of the transducer [27] where target closeness such as during transvaginal scanning may become crucial.[28] The TI algorithm assumes tissue perfusion is occurring.[29] Many scientist postulate that in humans, the major mechanism for respiratory gas exchange for most of the first trimester is diffusion, not perfusion. This poses a considerable additional problem in terms of the accuracy of the TI to reflect the true temperature change. With the advent of greater sensitivity of more recent Doppler devices there is some evidence of blood flow within embryonic vesicles following heart formation, and the simultaneous development of a uterine circulatory pathway in the developing placenta. The flow is often termed "non-pulsatile" or "percolating" [30, 31] with near-minimal Doppler-measured velocities, as opposed to later in pregnancy. At around week 12 of gestation there appears to be agreement that the plugs of the spiral arteries are "loosened" and allow for freer blood circulation.[32,33] Thus, perfusion status is far from approaching that for normal tissue levels (as assumed in the TI algorithm) for much of the first trimester. Only later when "free circulation" is established ($\geq$ ~ week 12 of gestation) does the tissue become perfused in the normal use of the term. This should lead to extreme caution in very early gestation, particularly with the recent increase in utilization of Doppler in the first trimester.[34, 35]

One of the most concerning aspect of the subject is the apparent lack of knowledge of the clinical end-users. Both in Europe[36] and the United States,[37] approximately 70% of clinicians (physicians and sonographers, including nurses who perform ultrasound) show very poor or no knowledge of bioeffects and safety issues, do not know what TI and MI represent and don't even know that these appear on-screen during clinical ultrasound examinations.

Non-thermal effects of ultrasound are probably negligible, if they exist at all, in the fetus. The major reason is that are no naturally occurring gas bodies in the fetal lungs and bowels and those are needed for cavitation to occur. It should be noted, however, that some non-thermal effects have been described in animals but at exposures well above the upper limit (MI = 1.9) imposed by the FDA.[38]

There is, in fact, very little information on energy output and exposure in clinical obstetrical ultrasound. Only recently has it been shown that, if one considers TI and MI to be some indication of acoustic output, then the levels are low in the first trimester,[39] second and third trimester,[40] Doppler studies,[41] although higher levels of TI can be reached in this modality, as well as 3D/4D examinations.[42] These studies should be viewed with some caution since they were performed in units where end-users were knowledgeable of bioeffects and safety. It should also be noted that in some countries, the number of prenatal ultrasound examinations has reached 10 per pregnancy and it is unknown whether there is a cumulative dose effect to exposure.[43] A recent issue of the Journal of Ultrasound in Medicine contained extensive articles on ultrasound fetal thermal[44] and mechanical[45] effects as well as an epidemiological analysis.[46]

The AIUM conclusions on epidemiology for obstetric ultrasound states that based on epidemiologic data available and on current knowledge of interactive mechanisms, one cannot demonstrate a causal relationship between diagnostic ultrasound and recognized adverse effects in humans.[47] However, the statement includes a very important element which needs to be kept in mind whenever examining any published data: all epidemiologic evidence is based on exposure conditions prior to 1992. This is the time when power outputs of ultrasound machines were allowed to substantially increase (see above). Finally, end-users need to pay attention to three important parameters that are under their control while performing a clinical study: the operating mode (which includes transducer choice), system setup and output control and the dwell time.

Regarding operating mode, B-mode carries the lowest risk, spectral Doppler the highest (with M-mode and color Doppler in between). Transducer choice will determine: frequency, penetration, resolution and field of view which all have impact on output. The system setup includes starting output power and image fine tuning performed by the examiner to optimize the image. These have no visible effect on acoustic energy (except if one follows TI and/or MI displays, see below). Controls such as focal depth, increasing frame rate, changing the sample volume in Doppler, all have a direct effect on acoustic power. A further complication is that different machines behave differently. It is therefore vital for each clinician to know his/her own machine. Receiver gain, however, has no effects. It often has similar effects to the above controls on the recorded image but none on the output of the outgoing beam and is, therefore, completely safe to manipulate. The third element is directly under control of the examiner: dwell time. It must be stressed again that dwell time is not taken into account in the calculation of the safety indices, nor, in general, until now, reported in clinical or experimental studies.

Maternal-fetal Bonding

The topic of maternal-fetal bonding has long been discussed in the obstetrical literature in general and, more particularly as related to diagnostic ultrasound.[48] Recently, several authors have published research demonstrating the advantage of 3D/4D ultrasound on maternal attachement to her unborn child. For instance, Pretorius et al.: "...Parents have a change in attitude regarding their fetus after undergoing 3D/4DUS. Mothers showed an increase in bonding to their fetus after 3D/4DUS in more categories than fathers".[49, 50] It is important to note that when examining earlier literature, i.e. before 3D entered the clinical arena, very similar analyses were performed for 2D ultrasound and these showed similar results.[51,52] In fact, identical findings of increased psychological attachment were described at a time when the images were far from being as clear as nowadays[53] Future fathers were also shown to be positively influenced by visualization of the fetus.[51] However, some have shown no effect[54] or even a negative aspect with increased anxiety and sense of vulnerability, both for 2D[55,56] and 3D.[57] Comparing 2D and 3D/4D, some authors have shown a clear advantage for the latter, for instance as demonstrated by mothers showing the 3D pictures to more people than 2D images [58] but many refute any advantage for 3D/4D. In a randomized study of 48 women, the addition of 4D ultrasound did not change significantly the perception that women had of their baby nor their antenatal emotional attachment compared with conventional 2D ultrasound.[59] Similarly Sedgmen et al showed that maternal-fetal attachment increased after both 2D and 3D ultrasound exposure.[57] Alcohol consumption showed significant reduction in the reported average number of drinks/week after visualizing the fetus but no significant difference in the pattern of change was noted for 2D compared with 3D ultrasound. Although mothers may express a preference for 3D imaging, this does not seem to have a significant impact on maternal-fetal bonding.[60] For all types of ultrasound, one of the main factors in parental perception is the feedback given by the examiner during the evaluation with high feedback resulting in significantly less anxiety and more positive emotional experiences, compared with those who received less feedback.[61,62] Again, note that these findings were already recorded more than 20 years ago.

Although it makes sense that visualizing the fetus almost in "real life" with 4D technology would improve attachment, particularly when seeing facial expressions,[63] it appears that 3D can, occasionally provide additional and more specific diagnosis in normal and high-risk fetuses. But no studies demonstrate specific positive (or negative) impact on clinical outcome and the evidence is rather weak of an advantage of 3D/4D over 2D for this particular subject.

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