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● *Invited Review*

NEONATAL CRANIAL ULTRASOUND: ARE CURRENT SAFETY GUIDELINES APPROPRIATE?

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Abstract—Ultrasound can lead to thermal and mechanical effects in interrogated tissues. We reviewed the literature to explore the evidence on ultrasound heating on fetal and neonatal neural tissue. The results of animal studies have suggested that ultrasound exposure of the fetal or neonatal brain may lead to a significant temperature elevation at the bone–brain interface above current recommended safety thresholds. Temperature increases between 4.3 and 5.6°C have been recorded. Such temperature elevations can potentially affect neuronal structure and function and may also affect behavioral and cognitive function, such as memory and learning. However, the majority of these studies were carried out more than 25 y ago using non-diagnostic equipment with power outputs much lower than those of modern machines. New studies to address the safety issues of cranial ultrasound are imperative to provide current clinical guidelines and safety recommendations. (E-mail: Michal.schneider@monash.edu) © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Cranial ultrasound, Fetal brain heating, Preterm infants, Thermal index, Mechanical index, Ultrasound safety.**

INTRODUCTION

Neonatal cranial ultrasound is the mainstay of modern management for prematurely delivered babies and those born after a complicated delivery involving episodes of hypoxia. The number of preterm births worldwide has steadily increased in the last 10 y, accounting for 11.1% of all live births (Blencowe et al. 2012). The developing brain of premature infants is vulnerable to injury in the early postnatal period (Ballabh 2010; Inder and Volpe 2000; Rorke 1992; Volpe et al. 2011). Cranial ultrasound is used routinely to monitor the development and complications of hemorrhagic and ischemic brain injury in these newborns in the weeks after delivery.

Despite the absence of ionizing radiation, ultrasound has the potential to cause focally induced temperature increases in the tissues being interrogated. Although several studies on this topic have emerged, only one review has been published to date specifically reporting on the implications of ultrasound-induced temperature increases on the developing neonatal brain in the human. To this end, we identified all relevant empirical studies on the physical interaction of ultrasound with developing neural tissue both *in utero* and during the postnatal period.

The focus of this review is on the relevance of the available evidence to the human neonatal brain and, importantly, on the clinical relevance of these studies for modern ultrasound machines.

PHYSICAL PARAMETERS OF NEONATAL CRANIAL ULTRASOUND

The potential for ultrasound to interact with biological tissue has been well established (Shankar and Pagel 2011). The scientific approach to establish safety assurance in diagnostic ultrasound was to consider the possible physical mechanisms that are responsible for biological effects during exposure to ultrasound. The two primary mechanisms involved in ultrasound bio-effects are thermal and mechanical effects. There has been substantial

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research into the thermal and mechanical effects of diagnostic ultrasound on soft tissue and bone, resulting in the implementation of the output display standards (ODS) and the ALARA (as low as reasonably achievable) principle (Barnett et al. 2000).

The ODS assumes linear propagation of ultrasound within a uniform, modestly attenuating tissue and displays thermal (TI) and mechanical indices in real time during the examination (Shankar and Pagel 2011). The TI is the ratio of the current acoustic power output from the transducer to the power required to cause a 1°C increase in temperature (Shankar and Pagel 2011). Three different thermal indices are used to estimate the temperature increase during a scan. These are the TIS, which is applied to exposure of soft tissues; the TIB, which assumes that a layer of bone is present in the focal region; and the TIC, which applies to the presence of bone (cranium) less than 1 cm from the skin (Shankar and Pagel 2011).

The mechanical index describes the relative potential for bio-effects associated with non-thermal mechanisms including cavitation (bubble formation in the presence of gas) (Shankar and Pagel 2011). Clinical safety statements have been published by governing bodies, expressing awareness that pulsed Doppler operates at maximum power outputs and has the greatest potential for biological effects (Barnett et al. 2000). These relate to the routine use of ultrasound for obstetric applications. There are no specific references to neonatal cranial applications. In particular, of the six major bodies that govern the safe practice of diagnostic ultrasound, only the British Medical Ultrasound Society (BMUS) has provided concise and detailed guidelines for the use of ultrasound during neonatal cranial examinations *via* the fontanelle. The BMUS safety guidelines incorporate a limit for the TI in conjunction with the duration of the neonatal cranial scan. They suggest that scanning time be restricted for any TI value >0.7. For a TI of 2.3, it is recommended that the duration of such scans be restricted to 4 min, and scanning of neonatal brain is not recommended for a TI > 3 (BMUS 2010). Although some fundamental research has evaluated the extent of ultrasound-induced heating in the brain, there are no reviews of the literature.

The absorption of energy in tissue leads primarily to a rise in temperature. The temperature elevation produced by ultrasound depends on the spatial peak temporal average intensity (I_{SPTA}), the ultrasound frequency, the dwell time along the beam axis, the width of the beam, the tissue properties, the individual patient and other minor factors.

The interface within the brain itself may be comparable to a fat–muscle or soft tissue–water interface. At these interfaces, only about 1% of the transmitted sound is reflected back to the transducer as echoes (Aldrich 2007). The remaining 99% of the sound energy is attenuated through scattering and absorption (Aldrich 2007). In practice, scattering is thought to contribute a negligible amount of attenuation. Attenuation of the ultrasound beam in soft tissue is a result primarily of the absorption of the acoustic wave motion by tissue, converting its energy to heat (Aldrich 2007; Rumack et al. 1998). The degree of absorption of the acoustic wave in neural tissue will depend on the frequency of the ultrasound beam (Lieu 2010). If the scan frequency is doubled, the attenuation is also doubled. Neonatal cranial scans are typically carried out using high frequencies within the range 10–15 MHz compared with the 2.5–5 MHz that is used for obstetric/fetal applications.

In a recent survey exploring worst-case power outputs as measured in water, the mean I_{SPTA} for B-mode imaging was 341 mW/cm^2, whereas it was 860 mW/cm^2 for pulsed Doppler and 466 mW/cm^2 for color flow Doppler (Martin 2010). Under the assumption of average acoustic and thermal parameters for soft tissue, the temperature rises calculated are given in Table 1 (Ter Haar 2011). In general, these temperature elevations are considered to be over-estimates, as they do not account for thermal conduction, the cooling effects of blood flow or movement of the transducer. However, in narrow, focused beams, such as those used in cranial examinations, the cooling effects of vascular perfusion are negligible (Duggan et al. 2000). Additionally, scanned beams heat less than stationary beams because of the reduced I_{SPTA} (Ter Haar 2011). The temperature rise during many diagnostic ultrasound examinations, such as obstetric/fetal applications, is limited by the use of scanned beams, with any point in tissue being interrogated for only a very short time. However, during neonatal cranial scans, the transducer remains stationary over the fontanelle with very minimal movement. Therefore, significantly elevated temperatures, such as those in Table 1, are more likely during cranial scans, based on the combination of a high frequency, stationary transducer and narrow beam, covering a very small surface area.

Table 1. Estimates of rates of temperature rise in soft tissue for different imaging modes*

Imaging mode	Mean I_{SPTA} (mW/cm^2)	Rate of temperature rise	
		°C/s	°C/min
B-Mode	341	0.048	2.88
Pulsed Doppler	861	0.123	7.38
Color Doppler	466	0.066	3.96

* These assume average acoustic and thermal parameters for soft tissue of absorption coefficient, μ_a = 0.06 neper/cm (0.5 dB/cm) at 1 MHz, and heat capacity, C = 4.18 J/g/°C.

Reprinted, with permission, from Ter Haar (2011).