Ultrasound in Med. & Biol., Vol. ■, No. ■, pp. 1–7, 2016

0301-5629/$ - see front matter

ELSEVIER

http://dx.doi.org/10.1016/j.ultrasmedbio.2016.01.002

● *Original Contribution*

BRAIN SURFACE HEATING AFTER EXPOSURE TO ULTRASOUND: AN ANALYSIS USING THERMOGRAPHY

Michal E. Schneider and Paul Lombardo

Department of Medical Imaging and Radiation Sciences, School of Biomedical Science, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, Victoria, Australia

(*Received* 22 *July* 2015; *revised* 5 *November* 2015; *in final form* 5 *January* 2016)

Abstract—Ultrasound is the imaging modality of choice to monitor brain pathologies in neonates after complicated deliveries. Animal studies have indicated that ultrasound may cause heating of brain tissues. To date, no study has explored brain surface heating by ultrasound during clinically relevant exposure. Hence, we investigated heating effects of B-mode and pulsed Doppler (PD) mode on *ex vivo* lamb brains using thermography. Five brains were scanned for 5 min in B-mode or for 3 min, 1 min, 30 s or 15 s in PD mode. Brain surface temperature was measured pre- and post-exposure using thermography. The highest mean temperature increase was recorded by B-mode (3.82 ± 0.43°C). All five PD exposure protocols were associated with surface temperature increases of 2.1–2.7°C. These outcomes highlight for the first time that B-mode ultrasound can contribute to brain surface heating during a routine cranial scan. Scan duration should be minimised whenever possible. (E-mail: Michal.schneider@monash.edu)   © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Cranial ultrasound, Heating, Thermal effects, Newborn.**

INTRODUCTION

The technology of ultrasound has advanced at a rapid rate over the last decade. Today, it can deliver increasingly high resolution images of detailed anatomy, as well as important functional information on blood flow in blood vessels using Doppler mode. Coupled with the lack of ionizing radiation and portability allowing bedside imaging, it comes as no surprise that clinicians are increasingly relying on this technology to diagnose and manage newborns in the neonatal intensive care unit. Ultrasound is of particular value in newborns delivered prematurely or at term after a complicated delivery involving episodes of hypoxia and fetal distress or after a traumatic instrumental delivery. Such newborns are at particularly high risk of hypoxic, haemorrhagic and inflammatory cerebral lesions (Correa et al. 2004; Limperopoulos et al. 2005; Srinivasan et al. 2006). Increasing evidence highlights the clinical usefulness of evaluating middle cerebral artery function as a predictor of adverse perinatal outcome (Gramellini et al. 1992; Jugović et al. 2007). Today, cranial ultrasound screening for premature or high-risk newborns is commonly carried out in neonatal intensive care unit wards around the world and is used to implement timely and appropriate management of the newborn. As such, cranial ultrasound has become a mainstay of modern neonatal care (van Wezel-Meijler et al. 2010).

There is no apparent consensus regarding cranial ultrasound scanning protocols or the timing of these examinations. A range of surveillance protocols have been proposed for premature newborns based on weight and gestational age at birth (Perlman and Rollins 2000). Such protocols commonly suggest that cranial scans be conducted as a matter of routine between postnatal days 3 and 5, between postnatal days 10 and 14, at day 28 and again at pre-discharge. However, some authors have recommended more frequent scans. In some institutions, the recommended number of cranial scans exceeds the proposed surveillance protocols and can be as high as 13 scans for babies born at 23–24 wk of gestational age until term equivalent age (Leijser et al. 2006). In 2001, the American Academy of Neurology recommended that neuro-imaging of newborns be performed once between post-natal days 7 and 14 and possibly repeated at 36–40 wk of gestational age (Ment et al. 2002). The problem with such a recommendation is that some

Address correspondence to: Michal E. Schneider, Department of Medical Imaging and Radiation Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University, Victoria 3800, Australia. E-mail: Michal.schneider@monash.edu

neonates may die within 24 h of birth, and in many cases such newborns will not have had a scan before death. The number of neonatal brain scans during the neonatal period has increased to minimise the risk of missing brain pathologies immediately after birth.

The newborn brain is usually scanned with the transducer placed directly on the anterior fontanelle (van Wezel-Meijler et al. 2010), and hence, there is no overlying bone to absorb incoming ultrasound waves and attenuate the energy (thermal and mechanical) associated with this technique. The power output emitted by the ultrasound machine during a scan is under the direct control of the operator. The output can be highly variable and, depending on the operators' practice, cranial scans may be carried out at exposure levels and durations that may exceed those proposed by professional societies. This is a concern given the evidence found in studies involving several animal models that ultrasound can adversely affect fetal brain tissue and can cause leakage of the blood–brain barrier in adults when combined with contrast material (Mesiwala et al. 2002; Vykhodtseva et al. 2006). Other adverse effects reported in animal studies include biologically significant heating, especially near the skull, with regularly recorded temperature increases of up to 4°C to 5°C (Barnett 2001; Bosward et al. 1993; Duggan et al. 1995; Horder et al. 1998a, 1998b), abnormal neuronal migration during gestational exposure in mice (Ang et al. 2006), disruption of axonal myelination in neonatal rats (Ellisman et al. 1987), cognitive effects on locomotor and learning behaviour (Devi et al. 1995; Suresh et al. 2002), as well as a reduction in memory function of fetal rats exposed *in utero* (Suresh et al. 2008). The important consideration to note here is that most of the early studies used older machines with significantly lower power outputs than those used in clinical practice today and focused on gross adverse effects, while ignoring the potential for subtle cognitive damage, such as memory loss and learning difficulties. Our group has found that chicks exposed to Doppler ultrasound for more than 3 min *in ovo* exhibit significant short- and long-term memory loss (Schneider-Kolsky et al. 2009). Our study used equipment that was until recently in clinical use. It is unclear what cellular mechanisms underlie such effects, but there appear to be links between the thermal and mechanical exposure to ultrasound and molecular/cellular perturbations in exposed brains, as well as the proximity of the insonated brain tissue to adjacent skull bone. A study of *in vitro/ex vivo* fetal guinea pig brains has reported that ultrasound exposure resulted in the highest temperature rises in tissues close to the skull bone (Bosward et al. 1993). The observed increases in temperature were positively correlated with increased gestational age and mineralisation of the skull bone.

The thermal effects of ultrasound on brain tissue have to date only been investigated using implanted thermocouples. There is no information on thermal exposure of ultrasound on the brain surface. Given that the transducer interface routinely heats up during scanning and because the neonatal brain is scanned directly *via* the fontanelle, without overlying bone to absorb any heating, it is important to establish to what extent the brain surface can heat during routine cranial scans (Duck et al. 1989). This issue is of particular concern when scanning very premature infants because the premature brain, in particular the germinal matrix vasculature where intraventricular haemorrhage commonly originates, is particularly sensitive to external stimuli (Ballabh 2010). The migration of neurons during fetal development is also sensitive to genetic, as well as biological, chemical and physical stimuli (Rakic 1990). Exposure of the mouse embryo to the mechanical and thermal effects of ultrasound has been found to affect neuronal migration and lead to inappropriate positioning of a subset of neurons in the cortical layer (Ang et al. 2006). We hypothesise that the brain surface will heat significantly during both B-mode and Doppler mode ultrasound. The aims of this study were therefore to investigate the surface heating of brain tissue with B-mode and Doppler mode at clinically relevant durations using infrared thermographic imaging.

METHODS

Brain tissue

Five fresh lamb brains (5–7 seven mo of age at slaughter) were purchased from a local abattoir. Lamb brains were chosen for this study as they are closest in size and weight to a premature human brain. *In vivo* modelling of such experiments is more difficult to carry out as creation of an artificial "fontanelle" or hole is required in the skull of newborn animals to mimic the clinical scanning of a newborn baby. The brains were kept refrigerated until 30 min before the experiments, when the brains were allowed to equilibrate at room temperature. The brain surface temperature outside the scanned area remained stable during the experiments.

Ultrasound of brain

The ultrasound machine used was a Philips HDI 5000 SonoCT (Philips Medical Systems, Bothell, WA, USA) with a C12-5 MHz curvilinear transducer. This machine was until recently in use in hospitals for obstetric and neonatal imaging. A "paediatric/cephalic" application setting was used in this study, together with a focal depth of 1–1.5 cm, 170 dB/C4 dynamic range, "low" persistence and frequency rate set at high. The derated maximum I_{SPTA} (intensity) of this transducer was reported as 118 mW/cm^2 for B-mode and 412 mW/cm^2