On the safety of elastography in fetal medicine: A preliminary study of hypoacusia

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Elastography is a promising technology to provide additional clinical information on the cervical effacement to that obtained from Bishop test and conventional cervicometry by ultrasounds. Among the different techniques, transient, or acoustic radiation force elastography (ARFE) is becoming the most common commercial elastography technique. However, the high intensity of thr beam that ARFE emits to generate the necessary concentrated burst of acoustic radiation [1] to induce a tractable shear oscillatory displacement (see Figure 1), has raised some concerns about its potential teratogenous effects during pregnancy. This letter is aimed at opening a debate to assess the safety of this type of elastography, and in particular to provide a preliminary screening of cochlear damage in exposed fetus.

The employed energy input by ARFE has not been tested when designing the current standard safety criteria, that is, the mechanical index (MI) related to the formation of bubbles by cavitation, and thermal index (TI) related to temperature elevation. In particular, fetal exposure to general ultrasound is limited by the US Food and Drug Administration (FDA) to a maximum spatial peak temporal average intensity of 720 mW/cm2 and maximum mechanical index of 1.9 [2]. Both indices are time-averages that do not capture orders of magnitude higher mechanical energy peaks concentrated during a few microseconds per second of operation (depending on the multi-frame elastography interval). Therefore, the possible

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harmful effects of such peaks of ARFE on particularly sensitive organs or structures have neither been evidenced nor disregarded in a conclusive way.

Few researchers have addressed the teratogenous effects of fetal elastography beyond comments in recent years, in particular a discussion held between K. Preis and G. Rus at the World Conference in Fetal Medicine 2016. Although they reported no apparent histological changes, the absence of other bioeffects could not be discarded and they recommended further studies. *In silico* simulations revealed that bone-tissue interfaces could concentrate thermal build-ups close safety thresholds [3]. The cochlea may be a particularly sensitive structure since ARFE is a mechanical pulsatile vibration, and the cochlea and semicircular canals are mechanically delicate organs that can be damaged by strong vibrations, as postulated by Fatemi et al. [4], as well as the brain.

In a previous study [5], we used elastography technique to quantify the cervical stiffness on a total of 42 pregnant women. Four years later, the teratogenous effect of ARFE is explored by a follow-up study of born children, focused on the outcomes of the neonatal hypoacusia screening test and medical records. The exposed population was compared to the reference population through a contingency table analysis to assess the excess of risk. The only positive case for hypoacusia was reported as a late premature (36 weeks, 1860 g), attributable to a Prader-Willi-like phenotype. Although no other hypoacusia cases were observed, the sample size provides no statistical significance (p-value=0.538) to conclude the harmfulness nor the safety of fetal exposure to ARFE. Given the recent concerns about the high intensity pulses required for acoustic radiation force, we call the scientific community to trigger a debate and further research on the safety of elastography in fetal medicine.

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References

[1] Rus, G. Nature of acoustic nonlinear radiation stress. Applied Physics Letters, 2014;105 (12), art. no. 121904

[2] Consensus Conference: The use of diagnostic ultrasound imaging during pregnancy. JAMA 1984; 252:669–672.

[3] Palmeri ML, Frinkley KD, Nightingale KR. Experimental studies of the thermal effects associated with radiation force imaging of soft tissue. Ultrason Imaging. 2004;26(2):100-14.

[4] Fatemi M, Alizad A, Greenleaf JF. Characteristics of the audio sound generated by ultrasound imaging systems. J Acoust Soc Am 2005; 117:1448–1455.

[5] Peralta L, Molina FS, Melchor J, Gómez LF, Massó P, Florido J, Rus G. Transient Elastography to Assess the Cervical Ripening during Pregnancy: A Preliminary Study. Ultraschall in der Medizin. 2015. DOI: 10.1055/s-0035-1553325.

Figure Legend

Figure 1. Schematic principle of ARFE.