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A new method for measurement of placental elasticity: Acoustic radiation force impulse imaging

M. Sugitani [a], Y. Fujita [a,*], Y. Yumoto [a], K. Fukushima [a], T. Takeuchi [b], M. Shimokawa [c], K. Kato [a]

[a] Department of Obstetrics and Gynecology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[b] Department of Anatomic Pathology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[c] Department of Cancer Information Research, Clinical Research Institute, National Kyushu Cancer Center, Fukuoka, Japan

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ABSTRACT

Introduction: The velocities of the lateral shear waves (Vs; m s^{-1}) generated by an acoustic radiation force impulse (ARFI) correlate with Young's modulus. Therefore, ARFI can be used as a new method to evaluate tissue elasticity. The aim of this study was to investigate the safety of ARFI imaging and the differences in placental elasticity in complicated cases.
Methods: The study population included 115 patients between 26 and 41 weeks gestation, who were divided into three groups, namely normal, fetal growth restriction (FGR) and pregnancy-induced hypertension (PIH). After delivery, the Vs values of the placenta were measured *ex vivo*. After ARFI imaging, microscopic examination was performed, the Vs values were compared among the three groups and the relationship between the Vs values and neonatal birthweight *Z*-score was investigated.
Results: No histological changes were noted even after ARFI imaging. The Vs values in the FGR group were significantly higher than those in the normal group (1.94 ± 0.74 and 1.31 ± 0.35 m s^{-1}, respectively; $p < 0.05$). The Vs values demonstrated a significant negative correlation with the *Z*-score. Moreover, as the *Z*-score became lower, the Vs values became higher in the range of *Z*-scores under −0.5 standard deviation (SD).
Discussion: We speculate that the increased Vs values in the FGR group may have been caused by histological changes, and that a more severe FGR might result in increased Vs values.
Conclusion: ARFI imaging was observed to have no apparent histological damage to the placental tissue. *Ex vivo* placentas from the FGR group were significantly more firm. Moreover, Vs values and *Z*-scores of birthweight had a significant negative correlation. Additional investigations are needed about the utility of this method for the evaluation of placental function *in vivo*.

1. Introduction

The evaluation of placental function is very important in the management of cases complicated by fetal growth restriction (FGR) and pregnancy-induced hypertension (PIH). In some cases, these conditions are recognised as causes of placental dysfunction. Although ultrasonography examinations, including Doppler flow studies, are widely used for placental evaluation, their clinical utility is still inadequate to detect placental dysfunction before delivery. In some cases of FGR and/or PIH, associated placental abnormalities such as infarction, inflammation and fibrosis are revealed by pathological analysis after delivery [1]. However, in some cases, the existence of pathological changes is unclear even after pathological examination.

Ultrasonography has recently been used to evaluate tissue elasticity [2]. One method of ultrasound-based elastography, acoustic radiation force impulse (ARFI) imaging, involves the use of a short acoustic push pulse in the target tissue, which causes a tissue displacement of approximately 1–20 μm. The displacement generates a lateral shear wave that propagates through the tissue during recoil, the velocity of which is expressed as Vs (m s^{-1}). As Vs correlates with Young's modulus, a known index of elasticity, the value of Vs is thought to reflect tissue elasticity, that is, faster shear wave speeds and smaller displacements are associated with stiffer tissues and slower shear wave speeds and larger displacements occur in more compliant tissues.

* Corresponding author. Department of Obstetrics and Gynecology, Graduate School of Medical Sciences, Kyushu University, Maidashi 3-1-1, Higashi-ku, Fukuoka 812-8582, Japan. Tel.: +81 92 642 5395; fax: +81 92 642 5414.
E-mail address: yfujita@med.kyushu-u.ac.jp (Y. Fujita).

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Table 1
Background characteristics of the patients enrolled in this study.

	Normal ($n = 74$)	FGR ($n = 24$)	PIH ($n = 17$)
	Median (range)		
Maternal age	32 (16–43)	33 (20–43)	34 (21–40)
Gravidity	1 (0–9)	1 (0–3)	1 (0–3)
Parity	1 (0–3)	0 (0–2)	1 (0–2)
BMI	23.4 (16.3–34.0)	24.4 (17.7–33.3)	26.3 (21.0–48.1)
sBP	111 (80–138)	123 (95–162)	151 (140–198)
dBP	63 (42–81)	73 (50–98)	96 (88–101)
GW at delivery	37.9 (32.7–41.4)	34.9 (26.3–38.7)	37.0 (30.4–40.3)
BW (g)	2778 (1860–3810)	1730 (440–2753)	2455 (1420–3790)
Z-score of BW (SD)	−0.02 (−1.41 to 1.54)	−1.87 (−3.53 to −1.48)	−0.7 (−1.40 to 1.59)
Apgar score (1 min)	8 (8–9)	8 (1–9)	8 (3–9)
Apgar score (5 min)	9 (8–10)	9 (4–9)	9 (4–10)

GW: gestational weeks; BMI: body mass index; sBP: systolic blood pressure; dBP: diastolic blood pressure; BW: birthweight.

To the best of our knowledge, no study has reported the use of ARFI technology on placental tissue; hence, we investigated the biological effects of ARFI on placental tissue *ex vivo* and evaluated the effect of the sampling site on ARFI measurements. In addition, as a preliminary study for the clinical use of this method to evaluate placental function in future, we investigated the difference in ARFI values of delivered placentas in cases with FGR and/or PIH.

2. Materials and methods

2.1. Study population

The study population included 115 pregnant women between 26 and 41 weeks gestation. In all cases, the gestational age was calculated from the first day of the last menstrual period and confirmed by ultrasound examination between 9 and 11 weeks gestation. All patients were Japanese and cared for at Kyushu University Hospital, and all gave informed consent to participate in this study. The ethical committees of Kyushu University Hospital approved the study protocol. Of the 115 patients, 74 were normal (normal group), defined as no maternal or fetal complications, except for pre-term birth. A total of 24 cases were diagnosed with FGR (FGR group), which was defined as an estimated fetal weight less than 1.5 standard deviations (SDs) below the mean, determined from Japanese standards for gestational age on ultrasonography [3]. A total of 17 cases were diagnosed with PIH (PIH group). Seven of the PIH cases were categorised as severe and the remainder as mild [4]. Eight cases complicated by both PIH and FGR were included in the FGR group. The clinical characteristics of the study population are shown in Table 1.

2.2. Measurement of the velocity of ARFI-generated lateral shear waves

The delivered placenta was covered with a plastic bag and placed in a test tank filled with water. Buffer material was placed between the placenta and the tank. Experiments were performed using a Virtual Touch Tissue Quantification unit with a 4C1 curved ultrasonography probe (2.0–4.5 MHz) (ACUSON S2000; Mochida Siemens Medical, Tokyo, Japan). Measurement of Vs was performed within a 1–3-cm region of interest (ROI) (Fig. 1A). Vs was measured five times in each region, and the mean value was determined using the method of analysis described below.

2.3. Analysis of the velocity of ARFI-generated lateral shear waves

2.3.1. Biological effects of ARFI on placental tissue ex vivo

To investigate the biological effects of ARFI on placental tissue, 50 consecutive measurements of Vs were obtained from each of the 10 full-term delivered placentas. These measurements were performed as soon as possible after the placentas were delivered. The placental tissue sample was housed in a rectangular chamber (5 cm × 2 cm × 4 cm) with the curved ultrasonography probe fixed above the chamber. Each measurement was taken from the ROI at a fixed depth of 2 cm (Fig. 2). Following Vs measurement, tissue samples were obtained from two areas for pathological examination and comparison: one sample from the area of the Vs measurement and the other from the area not subjected to ARFI in the same tissue samples. Specimens were fixed in buffered formalin, dehydrated and embedded in paraffin wax. Serial 3-μm sections of embedded tissue were stained with haematoxylin and eosin. Microscopic examination was performed by a single pathologist (T.T.) to document any evidence of tissue damage related to heating. In 10 randomised fields at a magnification of ×40, we defined positive evidence of tissue damage as the presence of histological changes in more than three fields.

2.3.2. Reliability of the Vs measurements

Repeat measurements of Vs were performed in each of the 10 delivered placentas from the normal group. The Vs values were independently measured 10 times in each placenta to calculate inter-observer (M.S., Y.Y. and Y.F.) and intra-observer (M.S.) intraclass correlation coefficients (ICCs). All examinations were performed using the same ultrasonography equipment (Siemens ACUSON S2000).

2.3.3. Comparison of placental elasticity in each region

The elasticity of the placenta as defined by the Vs values was measured and compared in the normal group. Placental tissue was sampled from three areas: the cord insertion region, intermediate region and marginal region of the placenta (Fig. 1B). In this study, the marginal region of the placenta was defined as the farthest region from the cord insertion region and the intermediate region was defined as the region between the cord insertion and marginal regions.

2.3.4. Comparison of placental elasticity among the three groups

To investigate whether the elasticity of the placenta differs among groups, the Vs values from the intermediate region were compared.

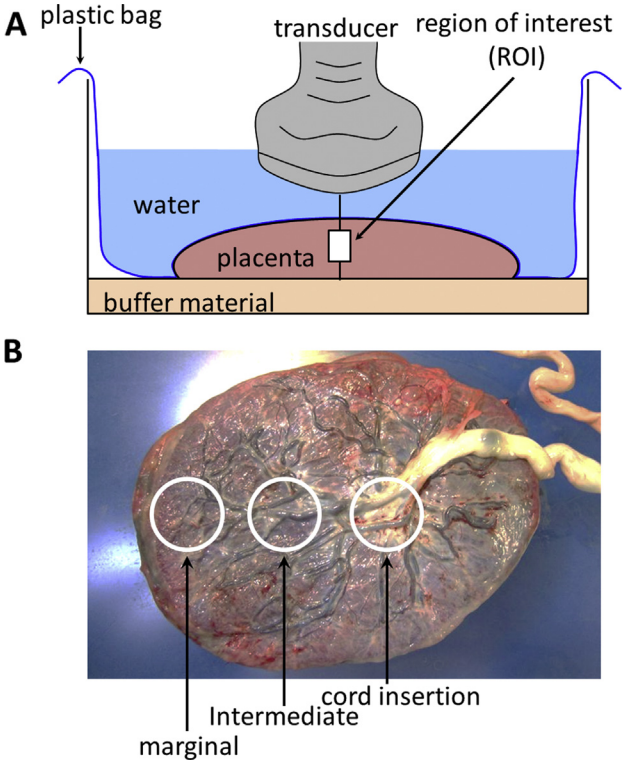

Fig. 1. A. Schematic of the experimental apparatus for the measurement of Vs. The delivered placenta was covered with a plastic bag and placed in a test tank filled with water. Buffer material was placed between the placenta and the tank. The Vs measurements were performed under the condition that the region of interest (ROI) was fixed within 1–3 cm. B. Placental regions of measurement.