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CORRECTED ARTICLE

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Visualization and quantitation of fetal movements by real-time three-dimensional ultrasound with live xPlane imaging in the first trimester of pregnancy

Aim To prove whether real-time three-dimensional (3D) ultrasound with live xPlane imaging is better in observing fetal movements than standard ultrasound imaging.

Methods 50 healthy women with singleton pregnancies (22-43 years old) at 11 to 14 weeks of gestation underwent real-time 3D ultrasound examination with live xPlane imaging from July 2014 to February 2015. The incidence and frequency of 10 fetal movement patterns in 10 minutes were evaluated, including general movements (GMs), isolated arm movements, isolated leg movements, hiccup, stretching, breathing, startle, jaw opening, isolated head retroflexion, and isolated head anteflexion. The correlation between gestational age and frequency of each fetal movement pattern was analyzed.

Results GM had the highest incidence (100%), followed by startle (84%) and isolated arm movements (68%). Their median frequency was 5 (IQR 3-6), 5 (IQR 1.75-11.5), and 1 (IQR 0-2), respectively. GM ($Z=5.875$, $P<0.001$) and startle ($Z=5.302$, $P<0.001$) had significantly higher frequency than isolated arm movements. The other 7 fetal movement patterns had much lower incidence and frequency. The frequency of GM was positively correlated with gestational age ($r=0.360$, $P=0.010$).

Conclusion Real-time 3D ultrasound with live xPlane imaging was shown to be a feasible tool for observing fetal movements.

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Fetal behavior is referred to as any observable fetal action, which may be observed by mother or recorded by real-time ultrasound (US) imaging. Fetal movements change with gestational age. There are rapid changes in position and posture at 9-12 weeks of gestation. In contrast, flexion and extension of the limbs, and longer episodes of changes in position occur at 13-16 weeks of gestation (1). An increasing number of studies have reported a discrepancy of fetal movement patterns between normally developing fetuses and the fetuses at risk (2,3). Also, assessment of fetal behavior could provide valuable data to differentiate normal brain development from abnormal brain development (4,5). Thus, fetal motility is increasingly considered a reflection of fetal neurodevelopment.

Fetal motility can be considered to be a spontaneous expression of the developing nervous system. The quantification of fetal movements has been shown to predict preterm birth and the absence of breathing movements served as a marker for preterm labor (6,7). The changes in the quality of general fetal movements identify the deterioration of the fetal central nervous system (8). Four-dimensional (4D) US technology has been applied to observe normal fetal facial expressions and fetal movements in all three trimesters (9). Nevertheless, it is limited by relatively low spatial resolution, staggering images, and a time-consuming procedure, which may affect the US biological effects and safety. The real-time three-dimensional (3D) processing facilitates simultaneous display of two high-resolution real-time images, thus acquiring a true midsagittal plane of the fetus (10,11). Real-time 3D echocardiography with live xPlane imaging has been used for scanning of the fetal heart (12). It is a simple and reliable method for assessment of fetal interventricular septum (13) and detection of fetal conotruncal anomalies (14). It has not been proved whether the real-time three-dimensional (3D) US with live xPlane imaging is a better method for observing fetal movements than US imaging.

In this study, real-time 3D US with live xPlane imaging was applied to observe and record the fetal movement patterns. Moreover, the incidence and frequency of each movement pattern was analyzed, and the correlation between frequency of each movement pattern and gestational age was evaluated. We attempted to prove the feasibility of the 3D US with live xPlane imaging in observing fetal movements.

PATIENTS AND METHODS

Patients

From July 2014 to February 2015, an observational study was conducted at the Department of Diagnostic Ultrasound and Department of Obstetrics and Gynecology of West China Women's and Children's Hospital. The study included 50 healthy pregnant women with normal singleton pregnancies who attended a routine US examination at 11 to 14 weeks of gestation. These women met the following inclusion criteria: no complications or clinical diseases; fetal crown-rump length (CRL) ranging from 45 to 84 mm; no abnormality detected by 2D US; normal fetal nuchal translucency (NT) measurement; delivery of neonates at term with normal 1- and 5-min Apgar scores (15). Exclusion criteria were pregnancies complicated by hypertensive disorders or congenital abnormalities; abnormal Apgar scores; preterm deliveries. The patients all offered signed informed consent before the study, which was approved by the ethics committee of West China Women's and Children's Hospital.

Methods

All patients underwent real-time 3D US examination with live xPlane imaging, performed by one experienced operator (Y.L) using iU elite 3D US machine (Philips, Bothell, WA, USA) equipped with a trans-abdominal X6-1 (6~1 MHz) matrix-array transducer. According to a previous research (16), the examination was performed by using manufacturer's NT preset, with mechanical index (MI) set at 0.4 and thermal index bone (TIB) set at 0.1. Following standard assessment in 2D B-mode US, the midsagittal view of a whole fetus was showed and zoomed as a region of interest, and the live xPlane function was activated. Subsequently, two real-time images of high-resolution were displayed simultaneously. The primary image plane was the midsagittal section of the whole fetus, displaying on the left part of the screen. The reference line was moved to the primary image line, and a secondary image plane cutting across the reference line was then exhibited on the right side of the screen. In the midsagittal section, the reference line was adjusted within the reference plane to be located along the fetal upper thorax. The axial section of the fetal upper thorax and arms (the secondary plane) was displayed in the right window. Because isolated arm movements might be missed in the midsagittal section, we chose axial section of the fetal upper thorax and arms as the secondary section. During the observa-

tion period, the probe was moved to both left and right parasagittal sections frequently, so as to avoid focusing on one section for a long time. The images displayed on the screen were recorded by videotape. The examination was performed for each participant in the same quiet room (temperature, 24-26°C).

According to the ALARA (As Low As Reasonably Achievable) principle (17), we determined the observation period to be 10 minutes. By analyzing the video recordings, we investigated 10 fetal movement patterns: GM, startle, stretching, isolated arm movements, isolated leg movements, hiccup, breathing, jaw opening, isolated head retroflexion, and isolated head anteflexion. Definitions of the 10 fetal movement patterns were in accordance with previous studies (5,18) (Table 1). Frequency and incidence of each fetal movement pattern during the observation period was evaluated by the same experienced observer.

Statistical analysis

Due to lack of controls, we did not perform the sample size analysis before the study. The SPSS statistical software (version 11.5) (SPSS Inc., Chicago, IL, USA) was used for calculations. Normality of data was tested by Kolmogorov-Smirnov test. Normally distributed data are expressed as mean \pm standard deviation (SD), otherwise as median with interquartile range (IQR). Differences were analyzed using *t* test or Wilcoxon signed ranks test. The Spearman's coefficient was used to assess the correlation between gestational age and the frequency of fetal movements. *P* value <0.05 was considered to be significant.

RESULTS

Participants

The mean maternal age of the eligible cases was 28.96 ± 4.15 (range 22-43) years, and the mean gestation age was 12.83 ± 0.82 (range 11-14) weeks. The mean NT and CRL values were 1.59 ± 0.38 (range 1.4-2.9) mm and 64.7 ± 10.6 (range 45-84) mm, respectively.

Observation of 10 fetal movement patterns

GM (Figure 1 A-B), startle (Figure 1 C-D), stretching (Figure 1 E-G), isolated arm movements (Figure 2 A-B), isolated leg movements (Figure 2 C-D), hiccup (Figure 3 A-B), breathing (Figure 3 C-D), jaw opening (Figure 4 A-B), isolated head retroflexion (Figure 4 C-D), and isolated head anteflexion (Figure 4 E-F) were clearly observed by real-time 3D US with live xPlane imaging.

GM (general movements) was the most common movement pattern with 100% of incidence (Table 2). It was observed in all 50 fetuses and its median frequency was 5 (IQR 3-6, range 1-7) times. Startle was observed in 42 of 50 fetuses (84%) and its median frequency was 5 (IQR 1.75-11.5, range 0-34) times. Isolated arm movement was observed in 34 of 50 fetuses (68%) and its median frequency was 1 (IQR 0-2, range 0-4) time. GM ($Z = 5.875$, $P < 0.001$) and startle ($Z = 5.302$, $P < 0.001$) occurred significantly more often than isolated arm movements, whereas there was no significant difference in frequency between GM and startle. The other 7 fetal movement patterns (stretching, isolated leg movements, hiccup, breathing, jaw

TABLE 1. Definitions of fetal movement patterns analyzed in the study

Movement pattern	Definition
General movements	Series of movements with variable speed and amplitude, involve all parts of the body without distinctive patterning of body parts. Duration varies from a few seconds to about a minute
Startle	Quick generalized movements, starting in the limbs and spreading to the neck and trunk, only last about one second
Stretching	A complex motor pattern, always carried out at a slow speed and consists of the forceful extension of the back, retroflexion of the head, and external rotation and elevation of the arms
Isolated arm or leg movements	Rapid or slow movements, and may involve extension, flexion, external and internal rotation, or abduction and adduction of an extremity, without movements in other body parts
Hiccup	A hiccup consists of a jerky contraction of the diaphragm
Breathing	Fetal breathing movements are usually paradoxical in a way that every contraction of the diaphragm causes an inward movement of the thorax
Jaw opening	The opening may be either slow or quick
Isolated head retroflexion and anteflexion	Isolated head retroflexion and anteflexion of the head not associated with general movements. Usually carried out slowly, but they can also be fast and jerky

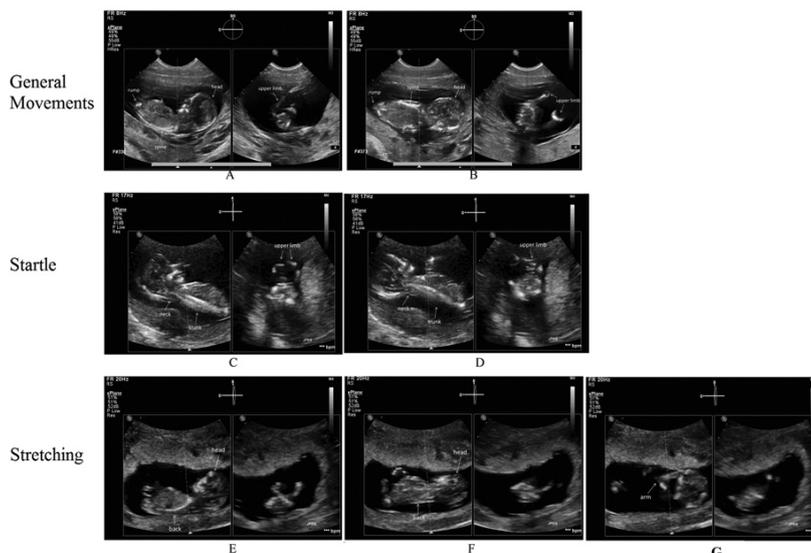


FIGURE 1. In-plane views of general movements, startle, and stretching by live xPlane imaging. **(A-B)** General movements involving the head, crump, spine, and limbs. **(C-D)** Startle. Quick generalized movement involving the neck, trunk, and limbs. **(E-G)** Stretching. Forceful extension of the back, retroflexion of the head, and elevation of the arms. The left side of each image is the primary image plane, while the right side is the secondary image plane (the axial section of the fetal upper thorax and arms). When the primary image is frozen, the original reference line disappears, thus the reference line in the primary image plane (left side) is added by the authors.

opening, isolated head retroflexion, and isolated head anteflexion) had a low incidence (10%-40%) and frequency (0), with varied frequency range during the observation period.

Correlation between the frequency of fetal movement and gestational age

Linear regression analysis was performed to evaluate the correlations between the frequency of each fetal movement pattern with gestational age (11-14 week). GM frequency showed significantly positive correlation with gestational age ($r=0.360, P=0.010$) (Figure 5). Frequency of the other 9 fetal movement patterns was not significantly correlated with gestational age.

DISCUSSION

In the present study, 10 fetal movement patterns were successfully detected by real-time 3D US with live xPlane imaging in 50 normal women with singleton pregnancies at 11-14 weeks of gestation. To our knowledge, this was the first time that real-time 3D US with live xPlane imaging was applied for observation and evaluation of fetal move-

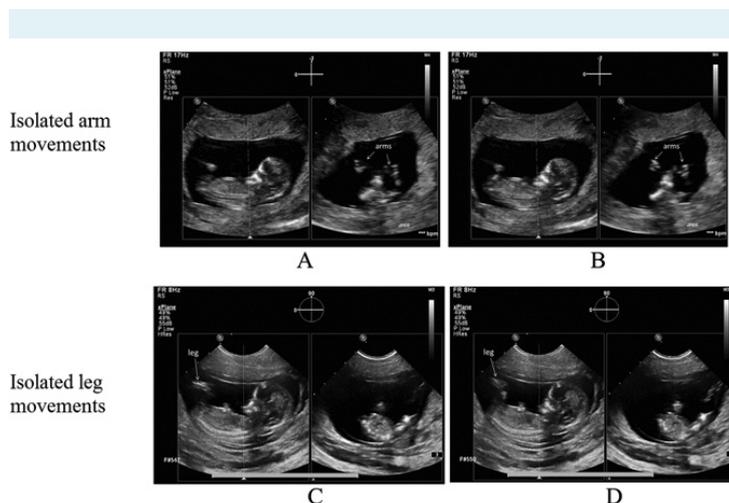


FIGURE 2. In-plane views of isolated arm movements and isolated leg movements by live xPlane imaging. **(A-B)** Movements of two arms are exhibited, without involvement of other body parts. **(C-D)** Isolated leg movements. Extension of one leg, without involvement of other body parts. The left side of each image is the primary image plane, while the right side is the secondary image plane (the axial section of the fetal upper thorax and arms). When the primary image is frozen, the original reference line disappears, thus the reference line in the primary image plane (left side) is added by the authors.

ments. Moreover, the study found that the frequency of GM was positively correlated with gestational age.

Evaluation of fetal movements could give useful insights into fetal functional characteristics and facilitate early detection of a range of prenatal neurological disorders and developmental dysfunctions (19,20). By using 4D US it is difficult to acquire a clear picture of specific movement patterns, such as hiccups, breathing, or jaw opening. Live xPlane imaging has been used to observe fetal heart chambers and aortic arches by providing high resolution view (21-23). Compared with conventional 2D US, real-time 3D US with live xPlane imaging adds another section and provides more information while the frame rate does not obviously decrease (24). With regard to the multiplanar view of 3D volumes acquired by conventional mechanical 3D probes, only the primary plane is acquired with full resolution while the other two planes are reconstructed. In contrast, live xPlane imaging displays two high-resolution real-time views of the target organ by using a matrix-array probe (11). In this research, the frame rate with live xPlane imaging was adjusted up to 19 Hz when zooming a whole fetus, enabling real-time visualization of fetuses in motion. The study suggests that it is a relatively simple and valid method for observation of fetal movements.

High-intensity focused US could effectively kill tumor cells and severely impair tumor blood vessels in human malignant carcinoma (25). Exposure to diagnostic US might lead to hyperthermia and tissue damage (26). Therefore, for fetal sonographic examinations safety issues are of utmost importance. Previous examinations of fetal movements using 4D US technology often took 15-30 minutes or longer (27-29). The present study determined the minimal exposure time and the lowest acoustic output that guaranteed

adequate diagnostic acuity of live xPlane imaging based on the ALARA principle (17,30). The fetuses were observed for a relatively shorter period (10 minutes), and for the sake of safety the MI and TIB of live xPlane imaging was set at 0.4 and 0.1, respectively (31).

The incidence of GM and startle was 100% and 84%, respectively, which was similar to the results of Hantoush-zadeh et al (90.8% and 74.2%, respectively) (32). Similarly, studies using 4D US have reported that GM is the most frequent fetal movement pattern (27,33,34). GMs emerge

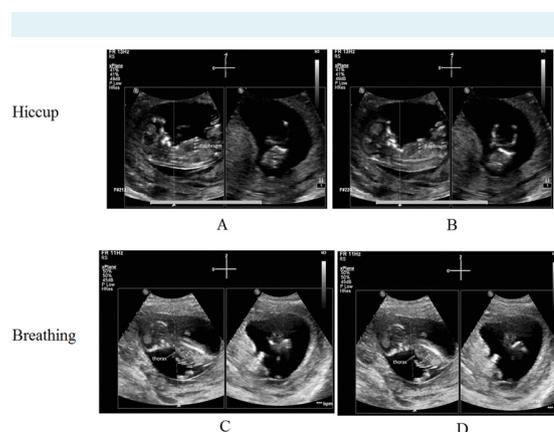


FIGURE 3. In-plane views of hiccup and breathing by live xPlane imaging. **(A-B)** Hiccup. A jerky movement of the diaphragm is seen. **(C)-(D)**, Breathing. The movement of the diaphragm and the inward movement of the thorax. The left side of each image is the primary image plane, while the right side is the secondary image plane (the axial section of the fetal upper thorax and arms). When the primary image is frozen, the original reference line disappears, thus the reference line in the primary image plane (left side) is added by the authors.

TABLE 2. Incidence and frequency of different types of fetal movement patterns*

Movement patterns	Fetuses (n)	Incidence (%)	Movement frequency range (times)	Median frequency (IQR)
General movements	50	100	1-7	5 (3-6) †
Startle	42	84	0-34	5 (1.75-11.5) ‡
Stretching	20	40	0-5	0 (0-1)
Isolated arm movements	34	68	0-4	1 (0-2)
Isolated leg movements	10	20	0-4	0 (0-0)
Hiccup	11	22	0-2	0 (0-0)
Breathing	18	36	0-4	0 (0-0)
Jaw opening	9	18	0-3	0 (0-1)
Isolated head retroflexion	5	10	0-2	0 (0-0)
Isolated head anteflexion	7	14	0-5	0 (0-0)

*IQR – interquartile range.

†Z = 5.875, $P < 0.001$, comparing general movements with isolated arm movements. ‡Z = 5.302, $P < 0.001$, comparing startle with isolated arm movements.

during early fetal life and are present until the end of the first half a year of life. They require the participation of all body parts, and are varied in intensity, force, and speed (35,36). Fetal onset of complex and variable GMs denotes the initiation of supraspinal modulation of spinal and brainstem circuitries. Perinatal assessment of GMs is a reflection of the integrity of nervous system (37). Fetal and infant GMs might provide useful information for predicting neurodevelopmental disabilities (38). This study found that of the 10 fetal movement patterns, GM was the only one movement pattern whose frequency was positively related to gestational age (11-14 week). Another study also reported that frequency of fetal movement patterns tends to increase with increased gestational age (28). Our result indicates that GMs might be used as a primary parameter for evaluation of fetal movements during 11-14 weeks of gestation. More studies are needed to disentangle the relationship between frequency of GMs and gestational age.

The limitation of this study is that it did not have a control group of patients (with abnormalities), nor did it have a control group with which it could be compared. The two sections obtained by real-time 3D US with live xPlane imaging could not include every part of the fetal body. Therefore, subtle fetal movements might not have been visualized in the midsagittal section or axial section of the fetal upper thorax and arms. This study only observed fetal movement during 11-14-week gestational period. Further studies should attempt to assess fetal movements in all three trimesters. Comparative studies with other alternative methods for observation of fetal movements are also required to yield more evidence supportive of application of live xPlane imaging. Additionally, fetal movements were analyzed by one sonologist and intra-observer agreement was not analyzed. The results obtained in this study should be validated by further studies including more sonologists with an acceptable degree of inter-observer agreement.

The study suggests that real-time 3D US with live xPlane imaging is a feasible tool for observation of fetal movements, compared with 4D US. GMs might be recommended as a promising variable for assessing the fetal movements at 11-14 weeks of gestation. Further studies are needed to verify the reproducibility and sensitivity of real-time 3D US with live xPlane imaging for perceiving fetal movements.

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Ethical approval received from ethics committee of the West China Women's and Children's Hospital.

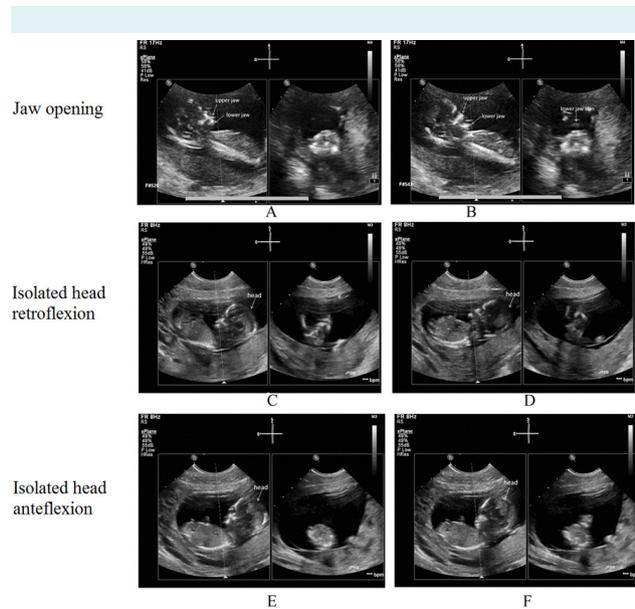


FIGURE 4. In-plane views of jaw opening, isolated head retroflexion, and isolated head antelexion by live xPlane imaging. (A-B) The opening of upper and lower jaw. (C-D) Isolated head retroflexion. Movement of other parts of the body is not seen. (E-F) Isolated head antelexion. Movement of other parts of the body is not seen. The left side of each image is the primary image plane, while the right side is the secondary image plane (the axial section of the fetal upper thorax and arms). When the primary image is frozen, the original reference line disappears, thus the reference line in the primary image plane (left side) is added by the authors.

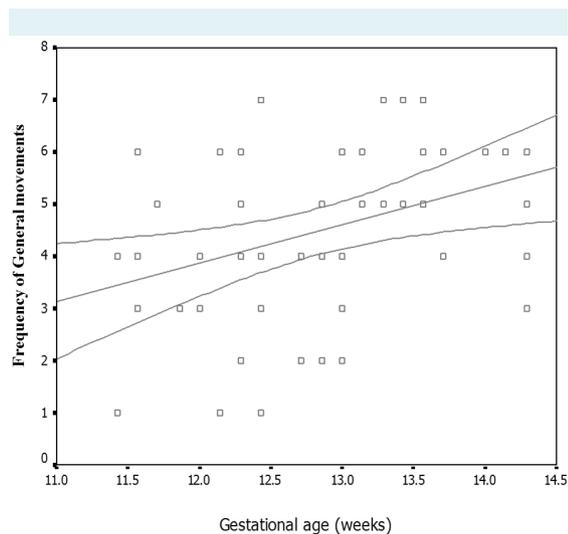


FIGURE 5. Scatter plot and linear regression analysis of frequency of general movement pattern vs the gestational age (weeks) ($y = -4.913 + 0.732x$; $r = 0.360$; $P = 0.010$). The frequency of GM was positively associated with gestational age ($r = 0.360$, $P = 0.010$).

Declaration of authorship YL contributed to the research design and performed real-time 3D US examinations. HL was responsible for the research control. TY recruited the participants. HS acquired and analyzed the data. FD and QC collected the important background information. WS drafted the manuscript.

Competing interests All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

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