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Cardiac vectors in the healthy human fetus: developmental changes assessed by magnetocardiography and realistic approximations of the volume conductor

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Abstract

This study sought to characterize the developmental changes of three measures used to describe the morphology of the fetal cardiac vector: QRS peak-amplitude, QRS duration and QRS time-amplitude integral. To achieve this objective, we rely on a recently developed methodology for fetal cardiac vector estimation, using multichannel fetal magnetocardiographic (fMCG) recordings and realistic approximations of the volume conductors obtained from *free-hand* ultrasound imaging. Fetal magnetocardiographic recordings and 3D ultrasound images were obtained from 23 healthy, uncomplicated pregnancies for a total of 77 recordings performed at gestational ages between 22 weeks and 37 weeks. We report the developmental changes of the cardiac vector parameters with respect to gestational age and estimated fetal weight, as well as their dependence on the estimated ventricular mass derived from cardiac dimensions measured with M-mode ultrasound. The normative values can be used along with the cardiac time intervals reported by previous fMCG studies to assist future clinical studies investigating conditions that affect fetal cardiac function.

Keywords

Cardiac vector; fetal magnetocardiography; boundary element method

1. Introduction

In the last decade, fetal magnetocardiography (fMCG) has emerged as an attractive non-invasive technique for *in-utero* assessment of cardiac function, allowing high resolution measurements of fetal cardiac electrophysiology from the second trimester of pregnancy to term (Comani *et al.* 2004, Horigome *et al.* 2000, Peters *et al.* 2001, van Leeuwen *et al.* 2004a, van Leeuwen *et al.* 1999, Wakai *et al.* 2003). Previous fMCG studies investigated the cardiac time intervals in healthy fetuses and demonstrated an increase in the duration of P wave and QRS complex with gestational age (Stinstra *et al.* 2002a, Horigome *et al.* 2000, van Leeuwen *et al.* 2004b). These changes reflect in part the increase in cardiac muscle mass

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associated with fetal growth. Although the increase in cardiac size throughout development should be also associated with an increase in signal strength, this relationship is less straightforward to be determined because the recorded signal amplitude is influenced by physical factors unrelated to cardiac electrophysiology, arising from the lack of control on the fetuses position and orientation relative to the sensing system, and from the variable geometry of fetal and maternal tissue compartments surrounding the fetal heart (Stinstra and Peters 2002b). Only a few studies have attempted to minimize these confounds by using source reconstruction techniques, which estimate the strength of the *primary* current sources, *i.e.* the fetal cardiac currents (Horigome *et al.* 2001, van Leeuwen *et al.* 2004a). However, the reconstruction algorithms were applied in simplified experimental settings by considering either half-space or spherically symmetric volume conductors, with *minimal or no* anatomical information about the fetal-maternal conductor. Although these simplified models permit closed-form analytical solutions of the forward problem and do not require imaging of the fetal-maternal unit, their restrictive assumptions may significantly affect the accuracy of the inverse biomagnetic solution (Stinstra *et al.* 2002b, Tao *et al.* 2012).

In this study, we used a recently developed approach for the estimation of fetal cardiac vectors which combines fMCG recordings and realistic approximations of the volume conductor obtained from individual 3D ultrasound images of the fetal-maternal anatomy (Tao *et al.* 2012). Our main objective was to derive improved estimators of the cardiac vectors and to obtain normative values for three quantitative measures of the cardiac vector morphology, *i.e.* the QRS peak-amplitude, QRS duration, and time-amplitude integral. Using recordings from 23 healthy pregnancies, we report herein the dependence of these parameters on gestational age and estimated fetal weight, as well as with respect to estimates of ventricular mass obtained from M-mode measurements of ventricular dimensions, from the end of the second trimester of pregnancy to birth.

2. Methods

2.1. Subjects and data acquisition

The data collection was part of a longitudinal study of fetal cardiac function using multichannel magnetocardiographic recordings. Twenty-three healthy pregnant women underwent a series of three to four visits from 22 to 36 weeks of gestation, for a total of 77 recordings. Among them, 17, 22, 21 and 17 recordings were performed at gestational ages in the ranges of 22–26, 26–30, 30–34 and 34–37 weeks of gestation, respectively. The study protocol was approved by the Human Subjects Committee of the Kansas University Medical Center. Informed consent was obtained from all participant mothers in the study.

The biomagnetic signals were recorded with an 83-channel fetal biomagnetometer (CTF Systems Inc., subsidiary of VSM MedTech Ltd.), housed in a magnetically shielded room. During the fMCG recordings, the pregnant women were asked to rest comfortably in a reclining pneumatic chair, which can be moved horizontally and vertically for optimal positioning under the cryostat. The spatial distribution of the axial gradiometer sensors with a 5 cm baseline ensures a full coverage of the maternal abdomen, with the cryostat being placed above the upper abdominal surface. For each subject, a continuous 4 minute recording (1200 Hz sampling rate and 0.5–200 Hz pass band filter) was acquired.

Ultrasound examinations were performed immediately prior to or immediately after the fMCG recording using a GE Logiq-P5 ultrasound system interfaced with a 4C 1.4–4.8 MHz wide band convex transducer. The objective of the ultrasound examination was threefold: to acquire 3D images of the fetal-maternal anatomical compartments that allow building realistic approximations of the volume conductors; to perform standard biometric measurements of the fetus to estimate the fetal weight; and to obtain morphometric

measurements of the fetal heart. To derive individual approximations of the volume conductors, we used the so-called *free-hand* 3D ultrasound, in which a 3D digitizer attached to the ultrasound probe records the positions and orientations of the probe for subsequent co-registration and reconstruction of the volumetric data. For this task, we used the Stradwin 3D Ultrasound Acquisition and Visualization software (Cambridge University, UK) and a TrakSTAR positioning digitizer system (Ascension Technology Corp., USA) attached to the ultrasound probe. The calibration of the probe-digitizer system was performed with an ultrasound phantom. For each subject, series of B-scan images were recorded by scanning the maternal abdominal surface from side to side and from the upper to lower abdomen for a total number of 5000 to 6000 frames per subject. Co-registration of the ultrasound images with the fMCG sensor array was accomplished using three fiducial markers placed at non-collinear locations on the maternal abdomen (right side, left side, and sternum). The center of the ultrasound probe was placed at the location of each marker, and the corresponding frames were recorded in Stradwin. These frames were later used to identify the marker locations on the volumetric image, but were excluded from subsequent processing. The marker positions relative to the fMCG sensors were determined in the biomagnetometer by localizing three coils placed at those locations.

Standard biometric measurements (*femur length, abdominal circumference and head circumference*) were performed using the features built into the GE Logiq-P5 ultrasound system. These measurements were used for subsequent estimation of the fetal weight using the Hadlock formula (Hadlock *et al.* 1984). During the same session, measurements of heart dimensions were performed by a pediatric cardiologist using M-mode images (figure 1). For this task, a four-chamber image of the fetal heart was acquired and the M-mode cursor was positioned perpendicular to the intra-ventricular septum under the atrio-ventricular valves, recording and storing a total of 6 to 8 cardiac cycles. The intra-ventricular septum thickness (IVSd), left ventricular chamber size (LVEDd) and left ventricular free wall thickness (LVPWd) were measured at end-diastole using the standard M-mode border measurement convention. The transverse heart diameter (TDd) was also measured from the anterior wall outer edge to the posterior wall outer edge at the maximum internal dimension of the ventricular endocardium. Adequate M-mode measurements were achieved only in 78% of the scans (60 cases). Unsuccessful M-mode screening in the remaining cases was due to suboptimal fetus positioning or poor image quality, which prevented the acquisition of 4-chamber view and/or positioning of the ultrasound beam perpendicular to the interventricular septum and ventricular walls. It must be noted that an unsuccessful M-mode screening in some subjects/gestational ages has reduced the number of recordings that could be used to assess the relationship between fMCG metrics and ventricular dimensions, but did not prevent using the corresponding fMCG data to characterize the relationship with gestational age and estimated fetal weight, since the standard biometric measurements (*femur length, abdominal circumference and head circumference*) used for this analysis were available from B-mode scans in all cases

2.2. fMCG data pre-processing

The fMCG signals were filtered using the Independent Component Analysis (ICA) Infomax algorithm in EEGLAB (Delorme and Makeig 2004). ICA has been applied previously in multichannel fetal magnetographic studies to extract and characterize contributions from spatially distinct electrophysiological sources (*e.g.* de Araujo *et al.* 2005, Mantini *et al.* 2006, Popescu *et al.* 2007, Popescu *et al.* 2008). When ICA is used for filtering purposes, the signal of interest is reconstructed in the sensors from a subset of independent components, *i.e.* after removing the components that show clearly identifiable temporal patterns corresponding to other sources (*e.g.* maternal cardiac activity). We adopted this approach to minimize the risk of fetal cardiac signal loss. At the next processing step, the fetal QRS

signals (R-peaks) were determined using a QRS detection algorithm relying on the cross-correlation of the signal with a manually selected QRS-template (Grimm *et al.*, 2003). Given that the duration of the recording was constant, the number of averaged beats varied according to differences in heart rate (mean value=554±47 beats, pooled across all subjects and gestational ages analyzed in this study). The presence of gross fetal body movements during the fMCG recordings was ascertained using actocardiography (Zhao and Wakai 2002). Specifically, gross body movements were defined when visually identified R-peak amplitude variations across independent components corresponding to fetal cardiac activity were associated with significant increases in fetal heart rate and changes in QRS morphology on the temporal segments before and after movement (figure 2). Vigorous body movements may cause trunk rotation or shifting of the cardiac source with respect to the sensing system. Since this increases also the risk for less accurate volume conductor modeling, the corresponding datasets were excluded from further analysis. Other fetal movements (due to, e.g., slight limb movements without a change in overall position) that were reflected only in brief, transient QRS changes, led to the automatic exclusion of the corresponding segments of data (as the corresponding QRS complexes were not passing the correlation threshold criterion). For all datasets with no indication of gross fetal body movements, the averaged fetal cardiac beat was estimated and used for the subsequent source reconstruction.

2.3. Ultrasound data analysis

We adopted a standardized approach to model the fetal body and amniotic sac (AS) compartments of the volume conductor (Tao *et al.* 2012). For each subject, we approximated the fetal body by merging an ellipsoid (fitted to the fetal trunk) and a sphere (fitted to the fetal head), determined from a set of fiduciary points and standard biometric measurements (head and abdominal circumferences). Similarly, we modeled the AS as an ellipsoid derived from a set of fiduciary points used to determine its long and short axes. This step was followed by an interactive local correction of the ellipsoid boundaries, as described in our previous report (Tao *et al.* 2012). The 3D ultrasound image volume was then re-sliced using fixed size planes oriented in the axial direction relative to the maternal abdomen. Re-sliced frames were saved along with the coordinates of the fiduciary points and were further processed in Matlab to determine the surface of the maternal abdomen. Following this, images were transformed to Analyze format (Biomedical Imaging Resource, Mayo Foundation) to allow for the segmentation and triangularization of the feto-maternal compartments performed with CURRY 5.0 (Compumedics Neuroscan). Triangularization of the boundary surfaces was done using average triangle sides of 5 mm, 10 mm, and 20 mm for the fetal body, AS and abdominal compartments, respectively. The source space was defined as a regular grid of points (3 mm spacing) inside the fetal trunk.

2.4. Source reconstruction

The gain matrix was computed using the boundary element method (BEM) with a linear-collocation approach (Mosher *et al.* 1999), which has been shown in previous feasibility studies to provide accurate solutions and efficient computational times (Tao *et al.* 2012). At early gestational ages (<28 weeks), we considered three-layer volume conductor models, with conductivities of 0.22, 1.4, and 0.05 S/m (Oostendorp *et al.* 1989, Stinstra and Peters 2002b) for compartments ascribed to the fetal body, amniotic fluid and surrounding tissues, respectively. For late gestational ages (>28 weeks), the source reconstruction results obtained with the three compartment model were contrasted against those obtained with a fourth compartment model, where a fourth layer with uniform thickness (5 mm) and conductivity of 2×10^{-6} S/m was added using a 3-D dilation of the fetal body compartment to account for the potential presence of vernix (Tao *et al.* 2012). The model providing a better fit to the measured data was selected for each individual case, given also that a goodness-of-

fit criterion was satisfied. This strategy was adopted to circumvent the lack of information about the presence and/or uniformity of the vernix. The implementation of the BEM in our study assumes nested volume conductor compartments; the existence of holes in the vernix that can affect the amplitude and distribution of the forward magnetic field (Stinstra and Peters 1998) is therefore expected to affect the goodness-of-fit for each of the two models tested. The quality of fit was evaluated by means of the explained data variance computed across all channels and over the whole QRS interval. The reconstruction results with explained data variance greater than 75% were considered to reflect a good fitting, whereas an explained variance between 50% and 75% was considered to reflect a moderate fitting. The data was discarded from the statistical analysis if the explained variance was lower than 50%.

The source reconstruction was performed using a recursive Multiple Signal Classification (MUSIC) algorithm (Mosher and Leahy 1998), which searches over the source space to find locations for which a linear combination of columns in the gain matrix projects onto the signal subspace, with a threshold subspace correlation set to 0.95. Once a dipole is identified, its gain is appended to a model matrix and the algorithm is repeated to search for another source. The rank of the signal subspace was selected by searching for a distinct drop in the magnitude of data matrix eigenvalues. The recursions stopped when the number of dipoles found was equal to the signal subspace rank, or when no more sources satisfying the threshold subspace correlation could be found. The dipole magnitudes were estimated by multiplying the data matrix by the pseudo-inverse of dipole gains matrix. The vector magnitude was subsequently derived by a vector summation of all estimated dipoles.

2.5. Statistical analysis

The metrics used to characterize the vector magnitude (VM) morphology were the QRS peak amplitude or *peak vector magnitude* (pVM), QRS duration, and QRS *time-amplitude integral* (TAI). The QRS complex was delineated manually (the analyzer was not blinded to the result), with the onset and offset identified on the reconstructed QRS traces as the first/last point marking a significant deviation in the signal slope from the PQ segment (for QRS onset) or ST segment (for QRS offset). The time-amplitude integral was determined as the area under the VM signal between the QRS onset and offset. A regression analysis (performed in *GraphPad Prism*) was used to characterize the relationship between each of these metrics and the gestational age, estimated fetal weight, and estimated total ventricular muscle mass, respectively. The total (left and right) ventricular muscle mass was estimated as:

$$TVM = \rho \cdot (V^{walls} + V^{IVS}), \quad (1)$$

where $\rho = 1050 \text{ g/cm}^3$ is the myocardial density (Myerson *et al.* 2002), and V^{walls} and V^{IVS} are the volumes of the outer ventricular walls and intra-ventricular septum, respectively. The volume of the ventricular walls was approximated by the difference between volumes of epicardial and endocardial shells, each approximated by prolate semi-ellipsoids with short (transverse axes) equal to TDd and TDd-2LVPWd, respectively:

$$V^{walls} = \frac{4}{3}\pi \cdot 0.5 \cdot \left[\frac{\alpha \cdot TDd^3}{4} - \frac{(TDd - 2LVPWd)^2(\alpha \cdot TDd - LVPWd)}{4} \right], \quad (2)$$

where the parameter α denotes the ratio of the outer ellipsoid long axis to its short axis and was considered $\alpha = 0.75$ based on the regression equations of the cardiac dimensions reported by Firpo *et al.* (Firpo *et al.* 2001). The symmetry of the adopted model is consistent with the fact that in the fetus the LV and RV face nearly the same systemic afterload, and, as a result,

the thickness of the free ventricular walls is essentially the same and the LV to RV mass ratio is close to unity (Bhat *et al.* 2004, Firpo *et al.* 2001). The volume of the intra-ventricular septum was approximated from the cross-sectional area of the inner ellipsoid multiplied by the IVSd:

$$V^{IVS} = \pi \cdot 0.5 \cdot \left(\frac{TDd}{2} - LVPWd \right) \cdot (\alpha \cdot TDd - LVPWd) \cdot IVSd \quad (3)$$

Two statistical models were tested for each cardiac vector metric, *i.e.* the commonly used linear regression model and a nonlinear power growth model. We tested the power model based on previous observations relating heart dipole moments to heart and body weight in animal studies (Nelson *et al.* 1975). Outliers were automatically identified and excluded in the fitting process using the ROUT method available in the GraphPad Prism (Motulsky and Brown, 2006). The model with the best goodness of fit was selected in each case based on the coefficient of determination. Mean values and standard deviation of the cardiac vector metrics were also estimated separately for gestational ages of 24, 28, 32, and 36 weeks, by grouping the sample data into 4 week-wide bins centered around these targeted gestational ages, and adjusting for gestational age using the corresponding regression equation.

3. Results

Out of the 77 total recordings, 12 recordings were discarded due to gross fetal body movements identified using actocardiography, and 1 recording needed to be excluded due to a co-registration problem. The retention rate was 76%, 86%, 81% and 88% for gestational age ranges of 22–26, 26–30, 30–34 and 34–37 weeks, respectively. Figure 3 exemplifies the reconstructed cardiac vector magnitude for the same subject at three gestational ages. The amplitude of the averaged QRS observed in the sensor signals exhibits significant variation across measurements at different gestational ages, which is associated to changes in the fetus positioning and source-to-sensors configuration. As a consequence of these changes, there is no obvious increase in the QRS peak-amplitude in the sensor-signals with gestational age. On the other hand, the reconstructed cardiac vector magnitude shows the expected increase in peak-amplitude, thus confirming that the source reconstruction can reduce the confounding effects introduced by a different positioning of the fetus relative to the sensors when measurements are repeated throughout gestation.

Out of the 64 recordings that were analyzed using the source reconstruction procedure, 14 datasets were characterized by a poor fitting (explained data variance lower than 50%) and were excluded from the regression analysis. Out of the 50 remaining cases, good fitting (> 75 % explained data variance) was obtained in 41 cases, and moderately good fitting (between 50 % to 75 % explained data variance) was obtained in 9 cases. Figure 4 shows the results of the regression analysis for the three cardiac vector metrics with respect to the gestational age and estimated fetal weight. The mean values of the cardiac vector metrics and cardiac dimensions measured in our study were adjusted for gestational age and are summarized in Tables 1 and 2, respectively. Two outliers identified for gestational ages after 28 weeks (characterized by high values of the peak VM) were excluded from the corresponding datasets. The 3-compartment model was more appropriate in 79% of the recordings performed after 28 weeks of gestation, while the 4-compartment model (including an uniform layer of vernix) was more appropriate only in the remaining 21%. No trend has been observed when comparing the goodness of fit for the 3- and 4-compartment models separately for gestational ages between 28 and 32 weeks and 32 to 36 weeks. Since the presence and uniformity of the vernix throughout gestation cannot be predicted on an individual basis, the model providing a better goodness-of-fit was selected on a case-by-case

basis as previously explained. Support for such an empirical approach comes also from previous studies investigating the vernix presence and distribution in large numbers of subjects (Visscher *et al.* 2005), which point out to a bimodal distribution, with most fetuses having a surface coverage of less than 10% or greater than 90% in late gestation.

Figure 5 (upper row of panels) illustrates the scatter plots of the three cardiac vector metrics versus the total ventricular mass and ventricular dimensions (LVPWd and TDd). The normal growth of the fetal heart assessed from M-mode measurements is generally associated with an increase in the peak-vector magnitude, QRS duration and TA integral. The ventricular dimensions obtained from M-mode measurements (summarized in Table 2) were in the range reported by other prenatal echocardiography studies (*e.g.* Tan *et al.*, 1992; Firpo *et al.*, 2001). As for the relationship with gestational age and estimated fetal weight, the corresponding r^2 values indicate that a relatively smaller variability in QRS duration can be explained by the estimated ventricular mass, LVPWd and TDd. The normative data on the relationships with LVPWd and TDd may sub-serve future studies using the reconstructed cardiac vector to investigate pathologic conditions, and are free of the geometric assumptions used in the estimation of the ventricular mass.

4. Discussion

The longitudinal study of 23 healthy pregnancies reveals a positive correlation of the amplitude and duration of the fetal cardiac vector magnitude with gestational age and estimated fetal weight from 22 to 37 weeks of gestation. The relationship between the peak-VM values obtained from fMCG and the estimated fetal weight resembles the one predicted analytically by studies in vertebrate animals (Nelson *et al.* 1975), which indicated a power growth model of the form $y = 3.43 \cdot x^{0.826}$. The exponent parameter of both models are in good agreement, yet the multiplicative constant (scaling factor) estimated in our study is higher (*i.e.* 4.64 vs. 3.43). This discrepancy can be partly due to the modeling approximations made by each study, including the assumed (default) electrical conductivity values of the volume conductor compartments. On the other hand, the peak-VM values obtained in our study are significantly higher compared to those reported by previous fMCG studies using simplified (spherical or half-space) volume conductor models (Horigome *et al.* 2001, van Leeuwen *et al.* 2004a). This confirms previous findings from simulation studies, which indicated that the simplified volume conductors may lead to underestimation of the VM (Tao *et al.*, 2012).

The mean QRS duration measured on the reconstructed cardiac vectors in our study shows an increase from 43.6 ms at 24 weeks to 50.5 ms at 36 weeks of gestation. These values are in the range reported by previous studies (Stinstra *et al.* 2002b), which used measurements of cardiac time intervals performed directly on the sensor signals. The increase in QRS duration with gestational age and fetal weight is consistent with the increase in ventricular mass; however, the *rate* of increase in QRS duration is significantly less than the rate of increase in ventricular mass. Furthermore, when compared to the cardiac vector strength, the corresponding r^2 values indicate that a relatively smaller variability in QRS duration is explained by fetal age, estimated fetal weight or ventricular mass. While these findings agree with observations from previous reports (*e.g.* Stinstra *et al.* 2002a), we cannot rule out that the signal processing (involving template matching and averaging) may lead to some distortion of the QRS waveform due to physiological beat-to-beat variability or trigger jitter (Schneider *et al.* 2001), which results in a smoothing effect following averaging.

In our study, we considered that the presence of vernix caseosa can affect the distribution of the magnetic field after 28 weeks of gestation. To address this aspect, we compared the 3-compartment model against the 4-compartment model and we found a significantly lower

success rate of the 4-compartment model across subjects. This can be partly due to the fact that the non-uniform coverage or the presence of holes in the vernix may considerably affect the accuracy of the 4-layer model with nested compartments, as indicated by previous simulation studies (Stinstra and Peters 2002b). A second objective of our study was to determine the success rate of the proposed methodology in providing good estimators of the cardiac vectors. The gross fetal body movement was found to be one factor that affects the success rate of the fMCG analysis. Using actocardiographic criteria, vigorous fetal body movements were observed in ~17% of the recordings. Real time ultrasound studies had reported that fetuses at early gestation tend to have more frequent transient body movements (Nasellopaterson *et al.* 1988). The fMCG recording time in our study was much shorter compared to the ultrasound study, and this may explain why we observed only a slight increase of the *overall* incidence of fetal body movement around 24 weeks of gestation. Another aspect that affects the overall success rate of the methodology arises from the fact that among the recordings with no evidence of fetal movement, ~21% did not provide appropriate goodness-of-fit according to the criteria used in our study. A low goodness of fit may be due to different factors, ranging from the geometrical and electrical conductivity approximations used in our approach to the fact that gross body movements were possible in some cases during the time interval when the fetus could not be monitored, *i.e.* between the fMCG recordings and ultrasound recording. Together with data affected by fetal body movements, this leads to an overall attrition rate of ~34%, which is acknowledged as a limitation of the methodology.

The normal range of the cardiac vector metrics reported in our study can assist future studies aiming to characterize the sensitivity of fMCG for identifying electrophysiological markers of fetal cardiac hypertrophy *in utero*. Since the cardiac vector magnitude depends on the myocardial mass, we posit that fetuses with cardiac hypertrophy may show abnormalities of the cardiac vector parameters. The peak vector magnitude and QRS integral appear more suited for such applications, since they exhibit a more significant dependency on the myocardial mass compared to the QRS duration. The increased risk for fetal cardiac hypertrophy is associated with a broad range of conditions, such as intra-uterine growth retardation, pulmonary valve and aortic stenosis, closure of the ductus arteriosus, tetralogy of Fallot, or maternal diabetes. The ultrasonographic fetal heart monitoring is the standard method in clinical settings, but additional investigational techniques, such as fMCG, may prove to have diagnostic value in cases of incomplete imaging due to factors like maternal obesity and/or suboptimal fetal positioning. For example, maternal obesity, which does not impact fMCG recordings (Peters *et al.* 2001, Comani *et al.* 2004), can prevent a complete fetal cardiac ultrasound imaging in nearly one third of diabetic pregnant women (Sekhavat *et al.* 2010). It is known that diabetes mellitus is associated with a high incidence of fetal cardiac hypertrophy (*e.g.* Rizzo *et al.* 1992; Veille *et al.* 1993; Ghandi *et al.* 1995), and therefore alternative approaches to ultrasound imaging would be beneficial in these diabetic obese pregnant women. The methods used in our study, however, rely on several approximations of the volume conductor and require additional investigations to characterize the sensitivity and specificity of the fMCG source estimators for the detection of cardiac hypertrophy. Due to the necessity of a simultaneous successful estimation of the cardiac vector parameters and confirmation of cardiac hypertrophy from echocardiographic examinations, a relatively high demand must be placed in such investigations on the number of enrolled subjects, as our findings show that this requirement may be only fulfilled in approximately half of the recordings.

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Figure 1.

Exemplification of a complete M-mode measurement performed in a fetus at 29 weeks, 2 days. The solid vertical white line marks the time of the diastole. The measured cardiac dimensions are shown on the left. LVPWd: left ventricular posterior wall dimension in diastole; LVIDd: left ventricular internal dimension in diastole; IVSd: interventricular septal thickness at diastole; RVIDd: right ventricular internal dimension in diastole; RVAWd: right ventricular anterior wall dimension in diastole; TDd: the transverse heart diameter in diastole.

Figure 2.

Identification of fetal movement using actocardiography. The exemplified fMCG signals were recorded in the third trimester of gestation (31 weeks and 2days). The upper trace shows a fetal cardiac independent component (IC), and the middle trace shows the R-peak amplitude trace. Signal variability due to fetal movement is noticed on the temporal segment shaded in yellow (around 60 sec) and is accompanied by fetal heart rate (FHR) acceleration (bottom trace).

Figure 3.

Exemplification of reconstructed cardiac vectors from fMCG recordings performed in the same subject at three gestational ages. Panels on the left show the volume conductor co-registered with the sensor array. The fetus was in cephalic presentation at 24 and 32 weeks and in a breech presentation at 28 weeks. The middle panels show the averaged fMCG data, and the right panels show the corresponding reconstructed vector magnitude (VM). The area under the QRS is shaded in gray.

Figure 4.

Developmental changes of the peak vector magnitude (VM, panels a, d), QRS duration (b, e) and time-amplitude (TA) integral (c, f,) are shown with respect to gestational age (upper panels) and the estimated fetal weight (EFW, lower panels). All scatter plots show the line of regression, and the 90% (continuous lines) and 95% (dotted lines) prediction intervals.

Figure 5.

Developmental changes of the peak vector magnitude (a, d, j), QRS duration (b, e, h), and time-amplitude integral (c, f, i) are shown with respect to the total ventricular mass (TVM), left ventricular posterior wall thickness (LVPWd), and heart transverse diameter (TDd), respectively. All scatter plots show the line of regression, and the 90% (continuous lines) and 95% (dotted lines) prediction intervals.

Table 1

Mean values of the fetal cardiac vector parameters adjusted for gestational age. Results were obtained using the reconstructed cardiac vectors with good or moderate fitting (50 out of 77 cases).

GA(weeks)	<i>n</i>	Peak VM (nAm)	QRS duration (ms)	TA integral (nAm s)
24	10	941.65 ± 331.38	43.58 ± 4.61	15.88 ± 7.29
28	14	1588.43 ± 745.78	44.61 ± 3.32	28.34 ± 14.25
32	15	2190.69 ± 607.35*	45.13 ± 6.01	50.50 ± 19.81
36	11	3840.21 ± 937.45*	50.58 ± 6.1	76.68 ± 34.71

* indicates one outlier was excluded from the corresponding data set

Table 2

Mean values of the morphometric fetal cardiac measurements adjusted for gestational age. Reported results were obtained from cases that were included in the regression analysis (fig. 5).

GA(weeks)	n	IVSd (cm)	LVPWd (cm)	TDd (cm)	TVM (g)
24	6	0.22 ± 0.055	0.24 ± 0.0588	2.24 ± 0.27	2.71 ± 0.83
28	14	0.28 ± 0.046	0.28 ± 0.042	2.83 ± 0.18	5.04 ± 1.15
32	11	0.32 ± 0.061	0.31 ± 0.08	3.25 ± 0.25	7.68 ± 1.57
36	10	0.38 ± 0.074	0.35 ± 0.066	3.91 ± 0.39	12.78 ± 3.38