ELSEVIER

Medical Engineering & Physics 25 (2003) 801–810

Medical Engineering & Physics

www.elsevier.com/locate/medengphy

Review

Review of electromagnetic source investigations of the fetal heart

Michael J. Lewis *

Department of Sports Science, Vivian Building, University of Wales Swansea, Swansea SA2 8PP, UK

Received 17 October 2002; received in revised form 6 June 2003; accepted 30 June 2003

Abstract

There is at present no reliable clinical technique for the assessment of cardiac electrophysiological activity in the fetus. There are two primary requirements of this type of monitoring: (i) sequential assessment of morphological and temporal parameters of cardiac electrical activity during advancing gestation, and (ii) description of the cardiac electrical activity in terms of an electrophysiologically realistic model. Fetal electrocardiography may be performed using maternal abdominal electrodes but this is only reliable prior to the 27th week of gestation. This is primarily because of the electrically insulating effects of the *vernix caseosa* and the existence of preferred conduction pathways between the fetal heart and maternal abdomen after this time. Fetal magnetocardiography is largely unaffected by these factors and so enables a reliable assessment of fetal electrocardiological activity throughout the second and third trimesters of pregnancy. This method can also be used to model fetal electrophysiological activity in terms of a current dipole or magnetic dipole. The vectorcardiogram is a plot of the dynamic change in dipole parameters during the cardiac cycle, allowing the study of growth-related or pathology-related electromagnetic changes in the heart. Fetal magnetocardiography and the fetal vectorcardiogram may thus provide important additions to current methods of antenatal monitoring.

Keywords: Fetal electrocardiography; Fetal magnetocardiography; Fetal vectorcardiography; Fetal heart; Antenatal monitoring

Contents

* Tel.: +44-1792-513043; fax: +44-1792-513171.
E-mail address: m.j.lewis@swansea.ac.uk (M.J. Lewis).

1350-4533/$30.00
doi:10.1016/S1350-4533(03)00121-8

1. Introduction

It is generally accepted that current methods of antenatal monitoring do not facilitate a comprehensive assessment of fetal well being. Consequently, there is continuing development of existing technologies and research into possible new methods that might improve current antenatal monitoring procedures. Antenatal monitoring seeks to assess several indicators of fetal status, including the pattern of fetal growth and maturation, oxygen availability, neurological function and cardiac function.

Although fetal heart rate (FHR) monitoring derived from ultrasonography is now routinely used for the assessment of cardiac rhythm, no technique for the specific assessment of cardiac electromagnetic activity has found routine clinical use. This is because fetal electrocardiography during the antenatal period (performed using electrodes attached to the maternal abdomen) is problematic. However, the magnetic analogue of this technique, namely fetal magnetocardiography, enables a more reliable assessment of the fetal heart's electromagnetic activity and may thus provide an important addition to current methods of obstetric care.

A clinically usable technique for the assessment of fetal electrocardiological integrity should facilitate the following: (i) sequential assessment of the relative magnitudes and temporal relationships of each phase of electrical activity during the cardiac cycle, and (ii) modelling of the electrical activity of the fetal heart in terms of physically and electrophysiologically realistic sources.

2. Fetal electrocardiography

The first fetal electrocardiogram (FECG) was demonstrated by Cremer [1]. Since that time, there have been many reported studies of the FECG during both the intrapartum (labour) and antenatal periods [2,3]. Several authors have observed that the amplitude of the FECG signals measured on the maternal abdomen between approximately the 27th and 35th week of gestation is severely attenuated [4–7]. The poor quality of electrical recordings during this period makes it difficult to observe sequential changes in the FECG during the third trimester of pregnancy. The FECG is also contaminated by the maternal ECG signal, although signal processing techniques can usually readily separate these two signals.

2.1. Temporal and morphological characteristics

Various attempts have been made to correlate the temporal characteristics of the FECG waveform with fetal status. The duration of the P wave has been reported to show a linear increase between the 17th week and full-term gestation [8]. The QRS duration has generally been observed to obey a similar trend, and this may be accounted for by the increase in ventricular mass during this period. Regular measurement during pregnancy of the duration of the fetal QRS complex may thus provide a method for the evaluation of fetal growth and status. It should be noted, however, that the QRS duration is proportionally larger in the fetus than in the adult, probably owing to structural differences in the His-Purkinje system in the fetus compared with in the adult [9]. Polvani et al. [8] reported a significant correlation between PR interval and gestational age, but only for fetuses between 17 and 20 weeks or between 37 and 41 weeks of gestation.

Rosén et al. [10] reported elevated T/QRS ratios in association with acidosis in the antenatal FECG for the fetal sheep. It has been proposed that the relative amplitudes of the FECG waves (such as P/R, Q/R, S/R and T/QRS ratios) may also provide an index for intrapartum fetal assessment [11]. However, there has been little further investigation of FECG waveform amplitude ratios during the antenatal period, particularly in the human fetus.

The FECG can also be used to measure the RR interval signal (the sequence of time intervals between successive R-waves), from which the FHR and its variability can be determined. Both of these parameters have generally been described as good indicators of fetal integrity. Pieri et al. [12] have described the development of an abdominal electrode FECG system from which FHR derivation was possible (implying a usable FECG signal) in around 65% of recordings in pregnancies after the 20th week of gestation. However, the authors noted that this success rate was reduced from around the 28th to the 32nd week and that it was highly variable for individual subjects.

3. Fetal magnetocardiography

The fetal magnetocardiogram (FMCG) is based on the measurement of the magnetic fields produced in association with cardiac electrical activity. The FMCG is recorded using the technique of SQUID (Superconducting Quantum Interference Device) biomagnetometry. Appropriately designed SQUID systems are highly sensitive to changes in magnetic flux density and are capable of substantial ambient noise reduction, making them well-suited for clinical FMCG measurement.

The FMCG has broad morphological and temporal similarity to the FECG. However, as the two methods are based on the measurement of two distinct quantities, namely the cardiac magnetic and electric fields, they may provide different (either complementary or unique) information. The FMCGs so far reported are generally of higher quality than most abdominal FECGs, with the

FMCG having the additional advantage of exhibiting virtually no maternal signal interference. Fig. 1(a) and (b) show, respectively, the raw and averaged FMCG data for a single fetus at various stages during the latter half (22–40 weeks) of pregnancy [13]. These data demonstrate the progressive change in morphology and improvement in signal-to-noise ratio of the FMCG signal with advancing fetal maturation.

3.1. Practical SQUID magnetometry

The FMCG is an example of a biomagnetic signal, the amplitudes of which are many orders of magnitude smaller than typical ambient magnetic fields (including the Earth's magnetic field). It is therefore instructive here to briefly consider the technique of SQUID biomagnetometry. The main aspects of the design and practical use of a SQUID-based magnetometer will be briefly reviewed.

When two superconductors are separated by a thin ($\sim 10^{-9}$ m thick) non-superconducting layer, a 'Josephson junction' is formed. The configuration of two Josephson junctions in a loop is the basis of the widely used 'DC SQUID'. When a vector potential is placed across a Josephson junction in a SQUID, the current flowing across it varies as a function of the magnetic flux passing through the SQUID loop. The SQUID magnetometer derives its name from this characteristic relationship between electrical current and magnetic flux. The SQUID system is designed so that the time-averaged voltage across the SQUID loop is also a periodic function of flux, effectively making the SQUID a flux-sensitive voltage output device. There are many comprehensive accounts of the theory of SQUID devices and their use in low frequency magnetic field measurements (for example [14]), and of their specific application in biomagnetism [15].

Biomagnetic measurements are usually carried out inside a magnetically shielded room (an enclosure with walls constructed from interleaved layers of materials with a high-permeability and a high-conductivity) but these are expensive and not readily available. Electronic noise suppression systems can be used to measure the ambient noise vector and thereby diminish low frequency (<2–3 Hz) noise. Detection coil arrangements known as gradiometers provide an affordable and practical means of spatially discriminating against distant noise sources in favour of nearby biomagnetic signals. In most SQUID-based magnetometers, the SQUID loop is placed within a superconducting shield and inductively coupled to the detection coil by means of a closed superconducting circuit known as a 'flux transformer'. The entire assembly containing the low-temperature components (SQUID sensor, gradiometer and flux transformer) is mounted on a cryogenic probe. The probe is inserted into a liquid helium dewar to maintain the temperature of the SQUID below the superconducting transition temperature. Fig. 2 shows the main components of a typical SQUID-based magnetometer (Cryoton UK Ltd.).

During practical biomagnetic recordings the SQUID magnetometer arrangement is positioned close to the anatomical region of interest. No part of the magnetometer is in contact with the body, and this eliminates

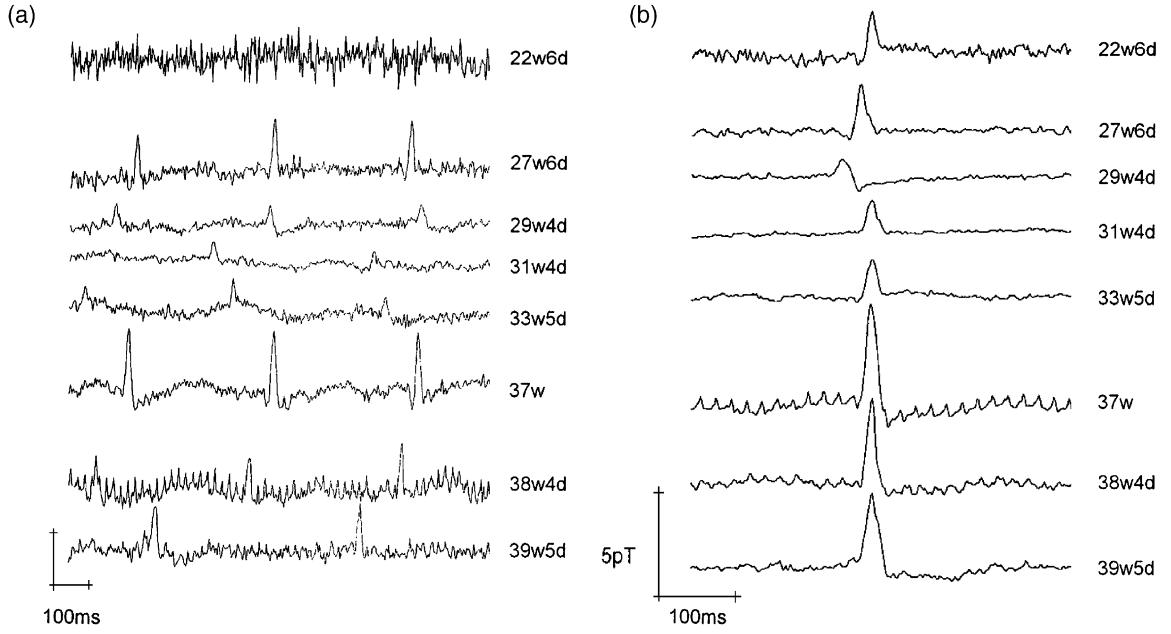

Fig. 1. (a) Raw FMCG data from a fetus at different stages of maturation [13]. Each data set is of 1.2 s duration. (b) Averaged FMCG data calculated from the data in (a) over a period of 25 cardiac cycles [13]. Each data set is of 0.5 s duration. Fetal age is indicated on the right (w=week, d=day).

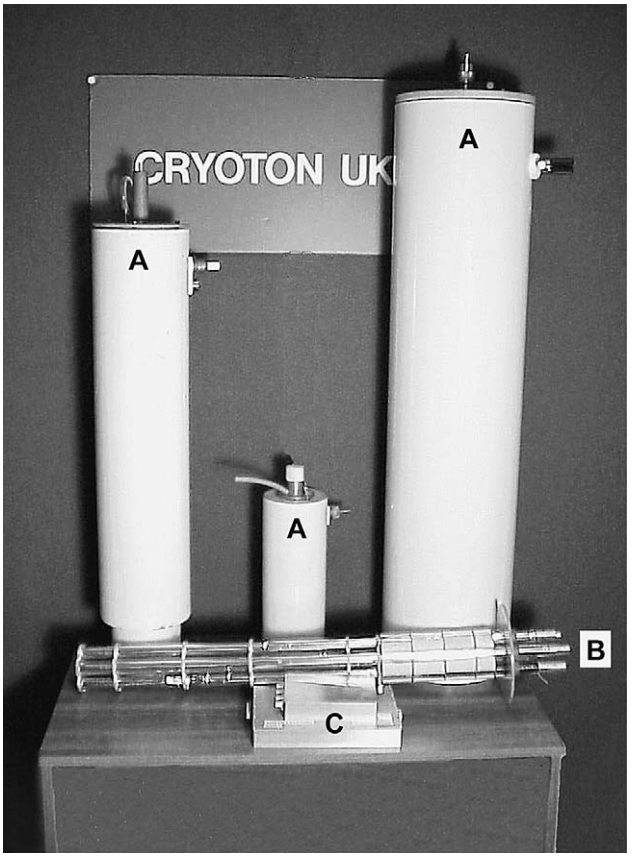

Fig. 2. Components of a multi-channel SQUID system: (A) a variety of cryogenic liquid helium dewars; (B) multi-channel cryogenic probes containing the SQUID sensors; (C) associated control electronics (courtesy of Cryoton UK Ltd.).

the problems associated with poor electrode contact and DC contact potentials. Fig. 3 shows a SQUID system positioned close to (but not touching) a pregnant mother's abdomen in order to detect the magnetic field produced by the fetal heart (Cryoton UK Ltd.). Of the three orthogonal magnetic field components, the one perpendicular to the body surface is usually measured as it is least influenced by differences in the electrical conductivities of body tissues.

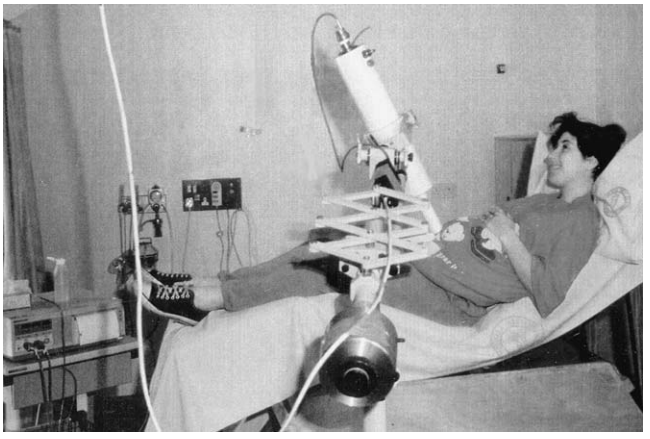

Fig. 3. SQUID system positioned close to a pregnant mother's abdomen in order to detect the magnetic field produced by the fetal heart (courtesy of Cryoton UK Ltd.).

The development of physical and mathematical models to describe and explain biomagnetic phenomena is an important aspect of biomagnetic investigation. The so-called 'biomagnetic inverse problem' is concerned with determination of the source of bioelectrical activity from the measured biomagnetic field. The most common approach to the solution of this problem is to approximate the current distribution (assumed to be localised according to realistic anatomical and physiological constraints) using a finite number of current dipoles of differing magnitudes and orientations [16,17]. The general form of a typical 'isofield map' of the magnetic flux density produced by the fetal heart, measured using a SQUID magnetometer, is shown in Fig. 4. Sarvas [18] has given a comprehensive review of the fundamental mathematical and electromagnetic concepts associated with the biomagnetic inverse problem.

3.2. Temporal and morphological characteristics of the FMCG

One of the earliest recordings of the FMCG was reported by Kariniemi et al. [19] using a SQUID biomagnetometer in a magnetically shielded room. The FMCG recordings showed all of the main waveforms associated with the normal adult MCG, although the maximum amplitude of the fetal signals (~5 pT) was an order of magnitude weaker than those obtained from the adult. Even from these preliminary studies, it was concluded that the FMCG was potentially a much better method than the FECG for electrocardiological monitor-

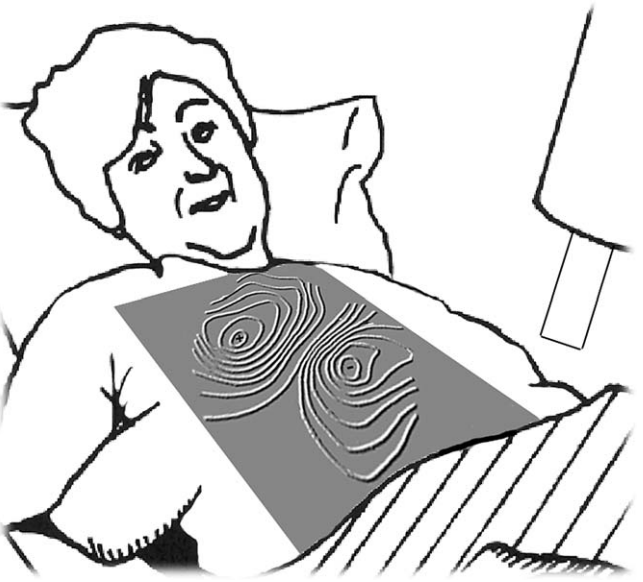

Fig. 4. Isofield map of magnetic flux density measured over a rectangular region of the thorax and abdomen.

ing during certain periods of gestation. The FMCG has since been successfully recorded and studied by a number of investigators [7,20–25], with Dunajski and Peters [7] reporting that an averaged FMCG could be derived from measurements made as early as the 13th week of gestation.

Kähler et al. [26] examined the temporal characteristics of the FMCG in 163 uncomplicated pregnancies. Significant correlations were observed between gestational age (in the period 21–42 weeks) and duration of the QRS complex, P wave and QT interval. Gestational age is also weakly correlated with PR interval in the period 17–41 weeks gestation [27] and with both PQ and QT intervals in the period after the 20th week of gestation [28]. Reductions in the duration of the P wave, PQ interval and QRS complex have been observed in intra-uterine growth retarded fetuses (IUGR, defined as a Doppler ultrasound-derived mass less than the 10th percentile) [29]. Golbach et al. [30] have presented reference ranges of the main temporal characteristics of the FMCG in uncomplicated pregnancies between 15 weeks and full-term gestation. These data were compiled from the pooled data of nine different FMCG research centres.

The source-detector distance has an effect on the amplitude of the recorded FMCG and so individual amplitudes do not in general yield clinically useful information. However, it is possible to meaningfully compare amplitude ratios, with the T/QRS ratio having received most attention. Wang et al. [24] and Van Leeuwen et al. [23] reported that the T/QRS ratio in the FMCG was approximately constant for different gestational ages, thereby suggesting its use as an index of fetal well-being, although Kandori et al. [31] found that the T/QRS ratio varied substantially in normal fetuses. However, it is generally difficult to determine the instant of T wave deflection from (and return to) the baseline level in the FMCG. (One possible explanation of this is that if the RT interval is variable then a signal averaging procedure that synchronises to the R wave of each cardiac cycle, a common procedure in many FMCG studies, would blur the features of the T wave [32].) This could affect the calculation of parameters involving the amplitude of the T wave, such as the T/QRS ratio. ‘Current arrow maps’ (which describe the spatial distribution of electrical activity) have been used to quantify the low-amplitude T wave in fetuses with prolonged QT syndrome [31], and this method might also be used to improve the calculation of the T/QRS ratio.

Van Leeuwen et al. [33] examined the utility of the FMCG for the diagnosis of fetal arrhythmias. These authors observed a variety of arrhythmic events (episodes of bradycardia, extrasystoles, supraventricular ectopic beats, bigeminy, trigeminy, SA block, AV conduction disturbances), concluding that the FMCG is suitable for the identification and classification of these anomalies. The FMCG has also facilitated the diagnosis of atrial flutter [34] and Wolff–Parkinson–White syndrome [35,36], these diagnoses being confirmed by neonatal ECG. Quartero et al. [37] demonstrated an uncoupling of the P wave and QRS complex in fetuses with complete AV block. These authors also found that the P waves of fetuses with atrial flutter were of greater amplitude than in uncomplicated pregnancies, and this was suggested to reflect atrial hypertrophy. It was concluded that the fetal MCG is superior to M-mode ultrasound in the diagnosis of fetal arrhythmia.

Several authors have reported the diagnosis of long QT syndrome using the FMCG [38–40]. Indeed, Hosono et al. [40] have indicated that the FMCG may be the most reliable tool for the prenatal diagnosis of long QT syndrome. The FMCG is the only modality that can be used to determine the duration of ventricular repolarisation in the fetus [41]. Ménendez et al. [41] have noted that the FMCG ‘could add substantial information to classify complex arrhythmias’, citing its capability of indicating both the source of ectopic activity and the severity of conduction abnormalities. FMCG mapping allowed Hosono et al. [42] to diagnose an alternating ventricular pacemaker in a case of complete AV block with QT prolongation (confirmed by postnatal ECG).

4. Effects of feto-maternal anatomy on electromagnetic source investigations

4.1. Volume conduction effects

The electrical impedance of tissue surrounding a source of bioelectrical activity can have a substantial effect on both the electric and magnetic fields measured external to the body. This ‘volume current’ effect [43] must be considered when interpreting these fields in terms of their electromagnetic sources. The simplest models of tissue conductivity assume a homogeneous, isotropic volume conductor format. More realistic inhomogeneous volume conductor models consist of discrete regions of tissue that are themselves homogeneous and are characterized by different electrical conductivities (or impedances). Electromagnetic investigations of the fetal heart have used models that consider the differing electrical conductivities of several different fetal and maternal tissues.

During the third trimester of pregnancy a protective covering known as the *vernix caseosa* develops around the fetus. This fatty substance, which appears as a covering on the skin of the newborn infant, protects the fetus from the *liquor amni*, the fluid surrounding the fetus within the uterus. The *vernix caseosa* has electrically insulating properties, with a resistivity that is substantially greater than that of the surrounding tissues and amniotic fluid [44]. The *vernix* therefore significantly attenuates the electrical potentials transmitted from the

fetal heart to the maternal abdomen. Other substances such as the amniotic fluid, blood and maternal abdominal tissues are also generally understood to affect the conduction of electrical signals from the fetal heart.

The FECG signal originates from both primary and volume currents in the heart, but the magnetic signal recorded near the maternal abdominal surface was originally thought to be associated with the primary cardiac current source alone [7]. This suggested that magnetic fields emanating from the fetal heart are not significantly affected by the presence of high electrical impedance tissues. It was therefore assumed that the FMCG would facilitate a more accurate analysis of the fetal heart's electrical activity than is available from the FECG.

Peters et al. [32] used finite-element and boundary-element models to investigate the influence on FMCG morphology of the volume conductor surrounding the fetal heart. It was reported that the *vernix caseosa* does in fact have an effect on the FMCG waveform. In an extension of this work, Stinstra and Peters [45] performed simulation studies of the effect of the volume conductor model on the FMCG produced by electric current dipole sources. These authors used magnetic resonance images of fetuses in the 36th week of gestation to create a single-compartment (homogeneous) and a three-compartment (inhomogeneous) model of feto-maternal anatomy. The three-component model (separately describing the fetus, amniotic fluid and maternal abdomen) was considered an appropriate model in pregnancies prior to the 28th week of gestation. However, a one component volume conductor was considered more appropriate during the later stages of pregnancy owing to the presence of the *vernix caseosa* (this model assumes there are no volume currents outside the vernix). The magnetic fields produced by current dipole sources using these two volume conductor models were compared with those using a half-space (semi-infinite homogeneous) model. Both volume conduction models produced markedly different results from the half-space model, implying that volume currents have a substantial effect on the FMCG. The authors concluded that an individual anatomical model might be needed for the accurate construction of the fetal vectorcardiogram. Further information regarding the effects of feto-maternal volume conduction has been obtained from comparative studies of the FECG and FMCG.

4.2. Comparative studies of the FECG and FMCG

Hukkinen et al. [5] demonstrated that in contrast to the observed monotonic increase in the amplitude of the FMCG signals with increasing gestational age, there is a marked decrease in the FECG signal amplitude measured on the maternal abdomen between the 27th and 35th week of gestation. Dunajski and Peters [7] compared their FMCG measurements on a small group of subjects with the FECG data of Oostendorp et al. [44]. A linear increase in the amplitude of the FMCG R-wave with increasing fetal age was observed, this increase being continuous throughout the period between the 27th and 35th week of gestation. These results were in marked contrast to the FECG data, which showed a marked reduction in amplitude during this period. Crowe et al. [46] investigated the relationship between the FECG and FMCG by performing both magnetic and abdominal electrode measurements on a 38-week-old fetus in an unshielded hospital ward. It was observed that FECG morphology is almost independent of electrode position. These FECG observations during the later stages of pregnancy are inconsistent with a volume conduction model of the fetal heart, in contrast with the situation prior to 28 weeks gestation [6]. Whilst variation in fetal orientation might be a contributing factor, it alone cannot account for these anomalous observations. Consequently, the concept of 'preferred conduction pathways' has been hypothesised.

Investigations of the anomalies outlined above led Kahn [47] and Roche and Hon [48] to suggest the existence of preferred conduction pathways (of low electrical impedance) for conduction of the cardiac electrical potentials between the fetus and the maternal abdominal surface between 27 and 35 weeks gestation. These pathways were attributed to the lower electrical impedance of the oronasal cavity/amniotic fluid pathway [48] and of the umbilical cord/placenta pathway [47] in comparison with the much larger electrical resistivity of the *vernix caseosa* which surrounds the fetus during this time. (The second of these pathways has since been discounted by Oostendorp et al. [44].) In this situation, the shape of the QRS potentials measured at different locations on the maternal abdominal surface would be very similar [6]. The non-uniform distribution of both the *vernix caseosa* and the amniotic fluid further complicate the situation as pregnancy progresses. The conductive patches which develop in the *vernix caseosa* during late gestation, while having a variable effect upon the FECG, have negligible influence on the FMCG [49].

An interesting investigation of the role of the *vernix caseosa* has been performed by Wakai et al. [50], who recorded the FECG and FMCG from a fetus with the condition *ectopia cordis* during weeks 26, 29 and 31 of gestation. This condition is characterised by the heart lying outside the chest wall and therefore the electric and magnetic signals from the fetal heart do not pass through the fetal skin and *vernix*. Several unusual observations were made regarding this subject: (i) FECG signal amplitude and the signal-to-noise ratio were very high; (ii) signal transmission properties of the FECG were consistent with a volume conduction model at each gestational age, with substantial spatial variation in signal morphology at different locations on the maternal abdomen; (iii) FECG signal amplitude increased

between 25 and 30 weeks gestation. The FMCG signal was similar to that of normal fetuses, but the spatial variation in morphology was more consistent with a homogeneous volume conductor model for the *ectopia cordis* fetus than for normal fetuses (confirmed by dipole location fitting using a homogeneous sphere model). This implied that the FMCG signal from a normal fetus is distorted by the skin and *vernix caseosa* to a certain extent.

5. Fetal vectorcardiography

5.1. Vector models of cardiac electrical conduction

It is assumed that the far-field electrical activity of the heart can be represented by an electric dipole that is spatially fixed but temporally variable in magnitude and orientation. This representation of the electrical activity of the heart is referred to as the 'equivalent current dipole' (ECD). A point ECD, which is assumed for the fetus, is identical to the clinical concept of the electric heart vector (EHV) [51]. Source parameters of the ECD (i.e. dipole moment and orientation) can be determined in the adult from electrical potential 'mapping' at the surface of the thorax. Lead field theory [52–55] can be used to reconstruct the ECD from both electrical potential and magnetic flux measurements, whilst the reciprocity theorem [56] can be used to model the 'equivalent magnetic dipole' (EMD) [57,58] from the measured magnetic flux. There is a close association between the ECD and EMD [58], but the two representations may give different (unique or complementary) information. Higher order models of cardiac electrical activity have also been investigated, including current and magnetic quadrupoles [59].

A plot of the dynamic temporal variation of the magnitude and orientation of the ECD or EMD during the cardiac cycle is known as a vectorcardiogram. Often vectorcardiogram analysis is restricted to the period of ventricular depolarisation (corresponding to the QRS complex of the ECG or MCG). Frank [60] and Spekhorst et al. [61] observed extensive spatial rotation of the equivalent cardiac dipole during the period of ventricular depolarisation for adults and children, as well as for full term and prematurely born infants. However, there have been few reports in the literature regarding investigation of the fetal vectorcardiogram (fetal VCG).

5.2. Summary of previous investigations

The first fetal VCG investigation of the human fetal heart was presented by Oldenburg and Macklin [6], using abdominal FECG data and a model consisting of a current dipole located within a homogeneous conductor. These fetal VCG loops showed extensive vector rotation (i.e. an 'open' shape) and a well-defined planar structure prior to 28 weeks gestation. These authors showed that the initially open loops became progressively more 'closed' as pregnancy proceeded. It was also suggested that the fetus in utero could be described in terms of a homogeneous volume conductor model during early pregnancy (before 28 weeks). However, the lack of spatial rotation of the ECD indicated that a non-uniform conduction model was more appropriate during later pregnancy. Oostendorp et al. [62] calculated the vectorcardiogram from abdominal electrode FECG measurements, assuming a homogeneous volume conductor model for the fetus/maternal abdomen and an ECD source of fetal cardiac electrical activity. Similar to the observations of Oldenburg and Macklin [6], the fetal vector loops obtained before the 28th week of gestation were described as 'open'. However, for pregnancies later than 32 weeks, the vector loops calculated in the fetal reference frame showed little spatial rotation.

Horigome et al. [63] used a nine channel SQUID magnetometer in a magnetically shielded room to estimate the magnitude of the ECD from the FMCG in 95 fetuses. These authors used a simple half-space model of fetal/maternal conductivity to determine the magnitude of the ECD [64]. The transverse diameter of the heart was determined from echocardiography (using a four chamber view), and this was compared with the magnitude of the ECD. In this way, the authors assessed both normal growth-related hypertrophic and cardiomegalic changes to the myocardium (such as occur in Galen malformation, endocardial cushion defect or twin–twin transfusion syndrome). The calculated dipole magnitude increased with advancing gestational age and showed a tendency to be greater in fetuses with cardiomegaly. The authors concluded that their method was suitable for the assessment of cardiac hypertrophy, but recognised that fetal (and dipole) orientation should also be considered when quantifying the ECD. These initial results suggest that the FMCG could provide both electrophysiological and anatomical information in a single assessment modality.

Rassi et al. [65] used a three channel SQUID magnetometer to record the FMCG from six normal fetuses of gestational age 29–38 weeks in a magnetically unshielded hospital ward. The ECD and EMD were modelled during the period of ventricular depolarisation using the reciprocity theorem and lead field analysis. Fetal VCG measurements in utero yield data in the maternal reference frame (rather than the fetal reference frame) and quantitative inter-individual comparison of vector loops is not possible unless accurate fetal anatomical information is available. (In this regard, a fetal frame of reference defined by the spinal axis and biparietal diameter, i.e. the diameter of the fetal head between the two parietal eminences, should be sufficient.) The three-dimensional vector loops calculated by Rassi et al. [65] were

therefore transformed into the 'maximum area reference frame' [6]. (The maximum area reference frame is identified by spatially rotating the fetal VCG loop to the orientation that has maximal area in the observer's line of sight. Subsequent three-dimensional coordinate transformation of the original vector (maternal reference frame) enables a standardised comparison of the vector loops from different fetuses.) The ECD and MCD vector loops demonstrated an open, 'near circular' planar structure for all subjects, with smaller 'tail loops' that were attributed to the Q and S waves. It was also observed that the ECD and EMD vector loops were approximately orthogonal, similar to the situation in the adult [58].

6. Discussion

There is evidence that fetal magnetocardiography might be a more appropriate method than the FECG for the evaluation of cardiac electromagnetic source parameters in the fetus. The existence of the electrically insulating *vernix caseosa* and preferred electrical conduction pathways diminish the utility of fetal electrocardiography during the later stages of pregnancy. Consequently, the FMCG is the only method that will permit a sequential assessment of cardiac electromagnetic source parameters as a function of gestational age throughout the second and third trimesters of pregnancy. Fetal magnetocardiographic data can also be readily transformed into a vectorcardiographic representation and thereby interpreted in terms of either the ECD or EMD.

Notwithstanding the apparent advantages of the FMCG compared with the FECG, it is important to consider the practical application of these techniques. Identification of appropriate recording locations is usually performed using ultrasonography prior to both FECG and FMCG recordings. Measurement of the FECG requires the relatively simple application of maternal abdominal electrodes and, apart from the smaller amplitude of the signals, the assessment is similar to recording an adult ECG. Recording the FMCG can be more problematic as we need to detect a magnetic flux density of the order 1 pT (10^{-12} T) in the presence of the much larger 'background' magnetic flux densities produced by the Earth ($\sim 10^{-4}$ T), large nearby metallic objects ($\sim 10^{-7}$ T) and even jewellery or metallic clothing fasteners worn by the patient. The biomagnetometer system used to detect the FMCG must therefore have the best possible sensitivity and noise-rejection capabilities. Preparation of a SQUID-based biomagnetometer prior to performing a magnetic measurement thus requires considerable technical skill; the cryogenic probe and dewar must be carefully set up and the electronic noise-canceling system must be properly 'balanced'.

Modern portable SQUID magnetometers suitable for recording the FMCG are substantially less expensive than the large multi-channel instruments used for detecting the magnetic fields produced by the heart and brain in the adult. However, the ongoing costs associated with both the employment of trained personnel and the purchase of consumables (mainly liquid helium) must also be borne in mind in evaluating the practical utility of the technique. Furthermore, biomagnetic measurements are usually performed in magnetically shielded rooms. From a clinical perspective this is usually inconvenient and often prohibitively expensive. However, Crowe et al. [46] and Rassi et al. [65] have proven that it is possible to successfully record the FMCG in magnetically unshielded environments throughout a substantial period of gestation.

There is ample scope for the continued investigation of fetal vectorcardiography. Of primary importance would be characterisation of the fetal vector MCG with advancing gestation during both normal and complicated pregnancies. Accurate determination of fetal orientation within the maternal abdomen (which is readily attainable using ultrasonographic imaging) would enable the vector loops to be defined in a standard 'fetal' reference frame. However, the development of more advanced mathematical models will also be necessary for evaluating the influence on the fetal vector MCG of fetal orientation, volume conductor geometry, measurement system configuration and non-dipolar source terms.

Differences in the morphology of the fetal VCG should enable a differential assessment of normal growth-related changes and pathological hypertrophy of the myocardium. The identification of possible correlation between changes in the fetal VCG and fluctuations in physiological variables such as neural activity, chemical imbalance, blood pressure, etc., would also be of interest. Future studies might also involve the investigation of morphological changes in the fetal VCG in response to remedial therapy, and a comparison of fetal and neonatal VCGs.

In summary, there is growing evidence to suggest that fetal magnetocardiography and fetal vectorcardiography represent valuable additions to current methods of antenatal monitoring. Further development of feto-maternal models of electromagnetic conduction, together with larger-scale clinical trials, should consolidate our understanding of the clinical utility of these techniques.

References

[1] Cremer M. Uber die direkte ableitung der aktiostromme des menschlichen herzens vom oesophagus und uber das elektrokardiogramm des fetus. Munchen Med Wochenschr 1906;53:811.
[2] Pardi G, Ferrazzi E, Cetin I, Rampello S, Baselli G, Cerutti S et al. The clinical relevance of the abdominal fetal electrocardiogram. J Perinat Med 1986;14:371–7.
[3] Crowe JA, Woolfson MS, Hayes-Gill BR, Peasgood W, Mohd-Ali MA, Huang Y et al. Antenatal assessment using the FECG

obtained via abdominal electrodes. J Perinat Med 1996;24(1):43–53.
[4] Bolte A, Bachman K, Kuhn G. Fetal heart action potentials and their diagnostic significance. A contribution to prenatal determination of maturity with the aid of fetal electrocardiography. Arch Gynäkol 1966;203(2):132–63.
[5] Hukkinen K, Kariniemi V, Katila TE, Laine H, Lukander R, Mäkipää P. Instantaneous fetal heart rate monitoring by electromagnetic methods. Am J Obstet Gynecol 1976;125:1115–20.
[6] Oldenburg JT, Macklin M. Changes in the conduction of the fetal electrocardiogram to the maternal abdominal surface during gestation. Am J Obstet Gynecol 1977;129:425–33.
[7] Dunajski Z, Peters M. Development of the fetal magnetocardiograms from the 13th week of gestation onward. In: Baumgartner C, Deecke, Stroink G, Williamson SJ, editors. Biomagnetism: fundamental research and clinical applications. Elsevier Science, IOS Press; 1995. p. 704–8.
[8] Polvani F, Brambati B, Pardi G. Analysis of the fetal ECG during pregnancy and labor. In: Crosignani PG, Pardi G, editors. Fetal evaluation during pregnancy and labour. New York, London: Academic Press; 1971. p. 22-1.
[9] Brambati B, Pardi G. The intraventricular conduction time of fetal heart in uncomplicated pregnancies. Br J Obstet Gynaecol 1980;87:941–8.
[10] Rosén KG, Greene KR, Hökegård K-H, Karlsson K, Lilja H, Lindecrantz K et al. ST waveform analysis of the fetal ECG. In: Monset-Couchard M, Karlberg P, Minkowski A, Oh W, Stern L, editors. Cardiovascular and respiratory physiology in the fetus and neonate, 133. Colloque INSERM/John Libbey Eurotext Ltd; 1986. p. 67–82.
[11] Deans AC, Steer PJ. The use of the fetal electrocardiogram in labour. Br J Obstet Gynaecol 1994;101:9–17.
[12] Pieri JF, Crowe JA, Hayes-Gill BR, Spencer CJ, Bhogal K, James DK. Compact long-term recorder for the transabdominal foetal and maternal electrocardiogram. Med Biol Eng Comput 2001;39(1):118–25.
[13] Lewis MJ. Fetal magnetocardiographic studies using a SQUID-based system. PhD thesis. University of Wales; 1996.
[14] Clarke J. Superconducting quantum interference devices for low frequency measurements. In: Schwartz BB, Foner S, editors. NASI series B: superconducting applications, SQUIDs and machines. New York: Plenum; 1977. p. 67–124.
[15] Katila T. Principles and applications of SQUID sensors. In: Williamson SJ, Hoke M, Stroink G, Kotani M, editors. Advances in biomagnetism. New York: Plenum Press; 1989. p. 19–32.
[16] Grynszpan F, Gaselowitz DB. Model studies of the magnetocardiogram. Biophys J 1983;13:911–25.
[17] Romani GL, Leoni R. Localization of cerebral sources with neuromagnetic measurements. In: Weinberg H, Stroink G, Katila T, editors. Biomagnetism: applications and theory. New York, Toronto: Pergammon Press; 1985. p. 205–20.
[18] Sarvas J. Basic mathematical and electromagnetic concepts of the biomagnetic inverse problem. Phys Med Biol 1987;32(1):11–22.
[19] Kariniemi V, Ahopelto J, Karp PJ, Katila TE. The fetal magnetocardiogram. J Perinat Med 1974;2:214–6.
[20] Kariniemi V, Katila TE. Perinatal magnetocardiography. In: Williamson SJ, Romani GL, Kaufman L, Modena T, editors. Proceedings of the 4th International Conference on Biomagnetism, 1982, Rome, Italy. Biomagnetism: an interdisciplinary approach. New York: Plenum Press; 1983. p. 299–310.
[21] Quinn A, Weir A, Shahani U, Bain R, Maas P, Donaldson G. Antenatal fetal magnetocardiography: a new method for fetal surveillance? Br J Obstet Gynaecol 1994;101:866–70.
[22] Wakai RT, Wang M, Martin CB. Spatiotemporal properties of the fetal magnetocardiogram. Am J Obstet Gynecol 1994;170:770–6.
[23] Van Leeuwen P, Lange P, Schüßler M, Lajoie-Junge L. Determination of changes in fetal cardiac time intervals and T/QRS ratio during pregnancy using magnetocardiography. In: Aine CJ, Okada Y, Stroink G, Swithenby SJ, Wood CC, editors. Proceedings of the 10th International Conference on Biomagnetism, 1996, Santa Fe (NM), USA. Biomag96. New York: Springer; 2000. p. 581–4.
[24] Wang M, Wakai R, Henry J, Forbes E, Martin CB. Fetal heart rate monitoring and waveform mapping of the fetal magnetocardiogram. In: Baumgartner C, Deecke, Stroink G, Williamson SJ, editors. Biomagnetism: fundamental research and clinical applications. Elsevier Science, IOS Press; 1995. p. 696–9.
[25] Zhuravlev YE, Rassi D, Emery SJ. Clinical assessment of fetal magnetocardiography. In: Baumgartner C, Deecke, Stroink G, Williamson SJ, editors. Biomagnetism: fundamental research and clinical applications. Elsevier Science, IOS Press; 1995. p. 700–3.
[26] Kähler C, Schleussner E, Grimm B, Schneider A, Schneider U, Nowak H et al. Fetal magnetocardiography: development of fetal cardiac time intervals. Prenat Diagn 2002;22(5):408–14.
[27] Leuthold A, Wakai RT, Martin CB. Noninvasive in utero assessment of PR and QRS intervals from the fetal magnetocardiogram. Early Hum Dev 1999;54(3):235–43.
[28] Horigome H, Takahashi MI, Asaka M, Shigemitsu S, Kandori A, Tsukada K. Magnetocardiographic determination of the developmental changes in PQ, QRS and QT intervals in the fetus. Acta Paediatr 2000;89(1):64–7.
[29] Van Leeuwen P, Lange S, Hackmann J, Klein A, Hatzmann W, Grönemeyer D. Assessment of intra-uterine growth retardation by fetal magnetocardiography. In: Nenonen J, Ilmoniemi RJ, Katila T, editors. Proceedings of the 12th International Conference on Biomagnetism. Biomag2000. Espoo, Finland: Helsinki University of Technology; 2001. p. 595–8.
[30] Golbach EGM, Stinstra JG, Grot P, Peters MJ. Reference values for fetal MCG/ECG recordings in uncomplicated pregnancies. In: Nenonen J, Ilmoniemi RJ, Katila T, editors. Proceedings of the 12th International Conference on Biomagnetism. Biomag2000. Espoo, Finland: Helsinki University of Technology; 2001. p. 595–8.
[31] Kandori A, Miyashita T, Tsukada K, Hosono T, Miyashita S, Chiba Y et al. Prenatal diagnosis of QT prolongation by fetal magnetocardiogram—use of QRS and T-wave current-arrow maps. Physiol Meas 2001;22(2):377–87.
[32] Peters MJ, Stinstra JG, van den Broeck SP, Huirine JAF, Quartero HWF, ter Brake HJM et al. On the fetal magnetocardiogram. Bioelectrochem Bioenerg 1998;47(2):273–81.
[33] van Leeuwen P, Hailer B, Bader W, Geissler J, Trowitzch E, Gronemeyer DH. Magnetocardiography in the diagnosis of fetal arrhythmia. Br J Obstet Gynaecol 1999;106(11):1200–8.
[34] Hosono T, Kanagawa T, Chiba Y, Neki R, Kandori A, Tsukada K et al. Fetal atrial flutter recorded prenatally by magnetocardiography. Fetal Diagn Ther 2002;17(2):75–7.
[35] Hosono T, Chiba Y, Shinto M, Kandori A, Tsukada K. A fetal Wolff–Parkinson–White syndrome diagnosed prenatally by magnetocardiography. Fetal Diagn Ther 2001;16(4):215–7.
[36] Kähler C, Grimm B, Schleussner E, Schneider A, Schneider U, Nowak H et al. The application of fetal magnetocardiography (FMCG) to investigate fetal arrhythmias and congenital heart defects (CHD). Prenat Diagn 2001;21(3):176–82.
[37] Quartero HWP, Stinstra JG, Golbach EGM, Meijboom EJ, Peters MJ. Clinical implications of fetal magnetocardiography. Ultrasound Obstet Gynecol 2002;20:142–53.
[38] Hamada H, Horigome H, Asaka M, Shigemitsu S, Mitsui T, Kubo T et al. Prenatal diagnosis of long QT syndrome using fetal magnetocardiography. Prenat Diagn 1999;19(7):677–80.
[39] Ménendez T, Achenbach S, Beinder E, Hofbeck M, Schmid O, Singer H et al. Prenatal diagnosis of QT prolongation by magnetocardiography. Pacing Clin Electrophysiol 2000;23(8):1305–7.
[40] Hosono T, Kawamata K, Chiba Y, Kandori A, Tsukada K. Pre-

natal diagnosis of long QT syndrome using magnetocardiography: a case report and review of the literature. Prenat Diagn 2002;22(3):198–200.
[41] Ménendez T, Achenbach S, Beinder E, Hofbeck M, Klinghammer L, Singer H et al. Usefulness of magnetocardiography for the investigation of fetal arrhythmias. Am J Cardiol 2001;88:334–6.
[42] Hosono T, Shinto M, Chiba Y, Kandori A, Tsukada K. Prenatal diagnosis of fetal complete atrioventricular block with QT prolongation and alternating ventricular pacemakers using multichannel magnetocardiography and current-arrow maps. Fetal Diagn Ther 2002;17(3):173–6.
[43] Nenonen J, Horacek BM, Katila T. Torso and heart models in magnetocardiography. In: Hoke M, Erné SN, Okada YC, Romani GL, editors. Biomagnetism: clinical aspects. Amsterdam, London, New York, Tokyo: Elsevier; 1992. p. 417–24.
[44] Oostendorp TF, van Oosterom A, Jongsma HW. The effect of changes in the conductive medium on the fetal ECG throughout gestation. Clin Phys Physiol Meas 1989;10(Suppl B):11–20.
[45] Stinstra JG, Peters MJ. The influence of fetoabdominal volume conduction on the fetal MCG. In: Nenonen J, Ilmoniemi RJ, Katila T, editors. Proceedings of the 12th International Conference on Biomagnetism. Biomag2000. Espoo, Finland: Helsinki University of Technology; 2001. p. 831–4.
[46] Crowe JA, Herbert JM, Huang XB, Reed N, Woolfson MS, Rassi D et al. Sequential recording of the abdominal fetal electrocardiogram and magnetocardiogram. Physiol Meas 1995;16:43–7.
[47] Kahn AR. Transmission characteristics in foetal electrocardiography. In: Proceedings of the 16th Annual Conference on Engineering, Medicine and Biology, Baltimore, USA, 5. 1963. p. 13-4.
[48] Roche JB, Hon EH. The foetal electrocardiogram V—comparison of lead systems. Am J Obstet Gynecol 1965;92:1149–59.
[49] Dunajski Z, Peters M. Volume current effects on the fetal magnetocardiogram. In: Hoke M, Erné SN, Okada YC, Romani GL, editors. Biomagnetism: clinical aspects. Amsterdam, London, New York, Tokyo: Elsevier; 1992. p. 565–9.
[50] Wakai RT, Lengle JM, Leuthold AC. Transmission of electric and magnetic foetal cardiac signals in a case of ectopia cordis: the dominant role of the vernix caseosa. Phys Med Biol 2000;45:1989–95.
[51] Karp P. Cardiomagnetism. In: Erné S, editor. Biomagnetism. Berlin: Walter de Gruyter; 1981. p. 219–57.
[52] Tripp JH. Physical concepts and mathematical models. In: Williamson SJ, Romani GL, Kaufman L, Modena T, editors. Proceedings of the 4th International Conference on Biomagnetism, 1982, Rome, Italy. Biomagnetism: an interdisciplinary approach. New York: Plenum Press; 1983. p. 101–39.
[53] Tesche CD. Analyzing multichannel magnetometer data. In: Koch H, Lübbig H, editors. Superconducting devices and their applications. Berlin: Springer-Verlag; 1992. p. 551–6.
[54] Tesche CD. Exploiting lead field analysis to obtain current source reconstructions and a figure of merit. In: Hoke M, Erné SN, Okada YC, Romani GL, editors. Biomagnetism: clinical aspects. Amsterdam, London, New York, Tokyo: Elsevier; 1992. p. 735–9.
[55] Hämäläinen MS, Ilmoniemi RJ. Interpreting measured magnetic fields of the brain estimates of current distributions. Helsinki University of Technology; 1984. Technical Report No. TKK-F-A559.
[56] Bastuscheck CM, Williamson SJ. Technique for measuring the ac susceptibility of portions of the human body or other large objects. J Appl Phys 1985;58(10):3896–906.
[57] Malmivuo J. On the detection of the magnetic heart vector—an application of the reciprocity theorem [dissertation]. Acta Polytechnica Scandinavica, Electrical Engineering Series 39. Helsinki: Finnish Academy of Technical Sciences; 1976.
[58] Barry WH, Fairbank WM, Harrison DC, Lehrman KL, Malmivuo JA, Wikswo Jr. JP. Measurement of the human magnetic heart vector. Science 1977;198:1159–62.
[59] Katila T, Karp PJ. Morphology and multipole presentations. In: Williamson SJ, Romani GL, Kaufman L, Modena T, editors. Proceedings of the 4th International Conference on Biomagnetism, 1982, Rome, Italy. Biomagnetism: an interdisciplinary approach. New York: Plenum Press; 1983. p. 237–63.
[60] Frank E. General theory of heart-vector projection. Circ Res 1954;11:258–64.
[61] Spekhorst H, Sippens Groenewegen A, Wilensky RL, Spaans R. Electrocardiographic body surface mapping. In: van Oosterom A, van Dam RTh, editors. Evolution of body surface potentials in the healthy newborn during the first week of life. Dordrecht: Martinus Nijhoff; 1986. p. 19–24.
[62] Oostendorp TF, van Oosterom A, Jongsma HW. The FECG throughout the second half of gestation. Clin Phys Physiol Med 1989;10(2):147–60.
[63] Horigome H, Shionon J, Shigemitsu S, Asaka M, Matsui A, Kandori A et al. Detection of cardiac hypertrophy in the fetus by approximation of the current dipole using magnetocardiography. Pediatr Res 2001;50(2):242–5.
[64] Williamson SJ, Kaufman L. Biomagnetism. J Magn Magn Mater 1981;22:129–201.
[65] Rassi D, Zhuravlev YE, Lewis MJ, Emery SJ. Vector fetal magnetocardiography. In: Aine CJ, Okada Y, Stroink G, Swithenby SJ, Wood CC, editors. Proceedings of the 10th International Conference on Biomagnetism, 1996, Santa Fe (NM), USA. Biomag96. New York: Springer; 2000. p. 533–6.