Recent Advances in Fetal Electrocardiography

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Abstract: Since the first observations of Cremer in 1906, fetal electrocardiogram (ECG) measurements via the maternal abdominal wall have remained a formidable challenge for clinical technicians and engineers in the cutting-edge field of information theory.

Previous obstacles in extracting fetal ECG still complicate their acquisition at the present. These include three main difficulties for non-invasive measurement of fetal ECG: first, the low signal to noise ratio; second, the lack of a standard lead system for fetal ECG on the maternal abdomen; and third, the factor of fetal movement or non-stationarity during recording. A new extraction system based on blind source separation with reference signals (BSSR) was utilized and our detection rates, both off-line (91%) and on-line (60%), in pregnancies of 20 to 41 weeks of gestation have shown a marked improvement from earlier attempts. With this development, we discuss the potentials and limitations of this new system.

Keywords: Accuracy of fetal ECG, accuracy of traditional Doppler cardiotocogram, advanced fetal electrocardiography, fetal arrhythmia, fetal ECG waveform, congenital heart defect.

1. INTRODUCTION

Since the first observations of Cremer in 1906, fetal electrocardiography (ECG) via the maternal abdominal wall has remained a formidable challenge for clinical technicians and engineers in the cutting-edge field of information theory [1, 2].

Previous obstacles encountered in extracting fetal ECG still complicate their acquisition at the present. There are 3 main difficulties preventing the non-invasive measurement of fetal ECG. First is the low signal (S) to noise (N) ratio which on average is less than 1. Fetal ECG has a voltage of 5-20 μV while maternal ECG (mECG) is about 1000 μV. In terms of amplitude, the fetal signal is less than 1/50 of the maternal ECG complex. In addition, other sources of high background noise such as the maternal electromyogram, the uterine electro-myogram and interference from the individual skin electrodes must be contended with. Especially between 28-34 weeks of gestation, fetal ECG voltage is known to decrease remarkably because of the enveloping vernix caseosa. To measure fetal ECG through the maternal abdominal wall can thus be likened to detecting ECG through a brick wall amidst very noisy surroundings. The second difficulty is the complex 3-D form of ECG. In adults, different ECG waveforms are observed according to assigned electrode positions. In the fetus, ECG is calculated from a chosen waveform (such as the lead II waveform) depending on fetal presentation and with the electrodes on the mother`s abdomen and not directly attached to the fetus itself. Finally, the third difficulty is associated with what is known as non-stationarity wherein due to fetal movement in utero, electric signals from each electrode change frequently. Therefore, in summary, measuring fetal ECG would entail extraction of a non-linear non-stationary 3-D signal from very complex mixed signals whose noise greatly exceeds the signal input [3].

In this study, we introduce a novel method to extract fetal ECG via the maternal abdomen and discuss its possibilities and limitations.

2. EXTRACTION METHOD OF FETAL ECG

As mentioned earlier, fetal ECG of at least 5μV is contained within a collective signal from electrodes on the maternal abdominal surface (Application Note of HP8040A Fetal Monitor, Abdominal ECG Monitoring, HEWLETT PACKARD). Extracting these 5μV signals from complicated noisy data truly a daunting task as compared to electroen-

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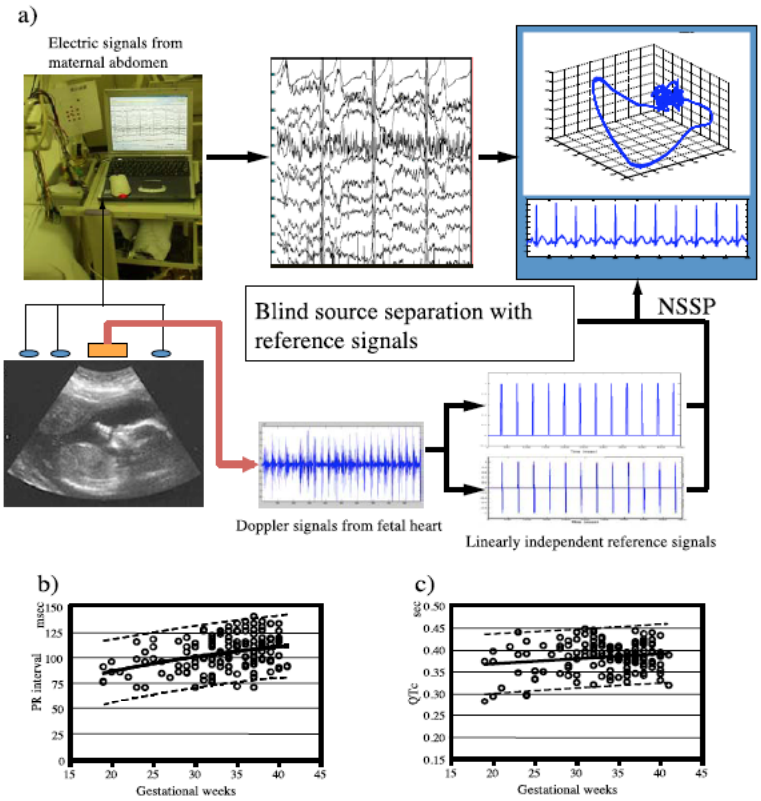

Fig. (1). The schematic diagram of our fetal ECG extraction system (**a**) and the standard values of PR intervals (**b**) and QTc (**c**) throughout gestation weeks. The terminal point of the T wave and the width of the P wave were calculated from averaged waves formed over 15 seconds of data with Doppler signals as reference [3, 7].

cephalography, for instance, where voltage is at least more than 30 μV.

There are two advanced methods commonly utilized: active adaptive signal processing and blind source separation (BSS) [2]. Our study method was Blind source separation with reference signals (BSSR) for extraction of fetal ECG which was based on BSS [3].

To understand this method, we can refer to a simple analogy. Imagine an astronaut whispering on the moon. The voice signal sent by the astronaut is so small and contaminated with large noise during its long conduction from the moon, so it would be impossible to hear it on earth. But using a method like BSS, the actual voice of the astronaut can be filtered through various transfer points (such as artificial satellites). At each transfer point, the small voice is mixed in with large noise but extraction is possible because these large noises are different for each transfer point. This is the principle of the BSS method. If the astronaut and the satellite system were changed into a fetus and a multichannel system of electrodes, we can extract the "whisper" of a fetus which in this case is the fetal ECG.

Our extraction method can also be explained from a mathematical point of view. Measured signals like ChA, ChB, ChC are mixed signals that include fECG, mECG and noise. So, simultaneous linear equations are given as:

$$ChA=a1 \cdot fECG+a2 \cdot mECG+noise1$$

$$ChB=b1 \cdot fECG+ b2 \cdot mECG+noise2$$

$$ChC= c1 \cdot fECG+ c2 \cdot mECG+noise3$$

We can calculate fECG as a solution of those linear equations.

In cases where there is large noise contamination, fetal ECG extraction is sometimes difficult with the BSS method alone. The BSS method is not stable in this case, because its algorithm tends to extract a common part of collective noise over observation signals instead of tiny fetal ECG. On the other hand, BSSR is more stable. This method has been improved by the addition of a learning process with reference signals such as eliciting the about timing or allowing for shape mimicry of fetal ECG. For instance, if the lead II ECG waveform is desired, then the lead II shape is adapted as a reference signal for fetal ECG extraction. Moreover, there can be more than one reference and this can be from a fetal heart source such as continuous Doppler signals. An algorithm for our fetal ECG system is shown in Fig. (**1**).

3. RECENT RESULTS OF OUR FETAL ECG SYSTEM

3.1. Normal Data

We studied 179 pregnant women with singleton pregnancies from 18- to 41-weeks gestation. Fetal signals were successfully detected in 163 out of 179 subjects at a 91.1% success rate regardless of fetal movements. PR intervals and QTc were calculated (Fig. **1**, **b**, **c**) [4].

3.2. Fetal Arrhythmia

At present, premature atrial contractions (PAC), premature ventricular contractions (PVC) and the sick sinus syndrome (SSS) can be detected using fetal ECG, but it remains

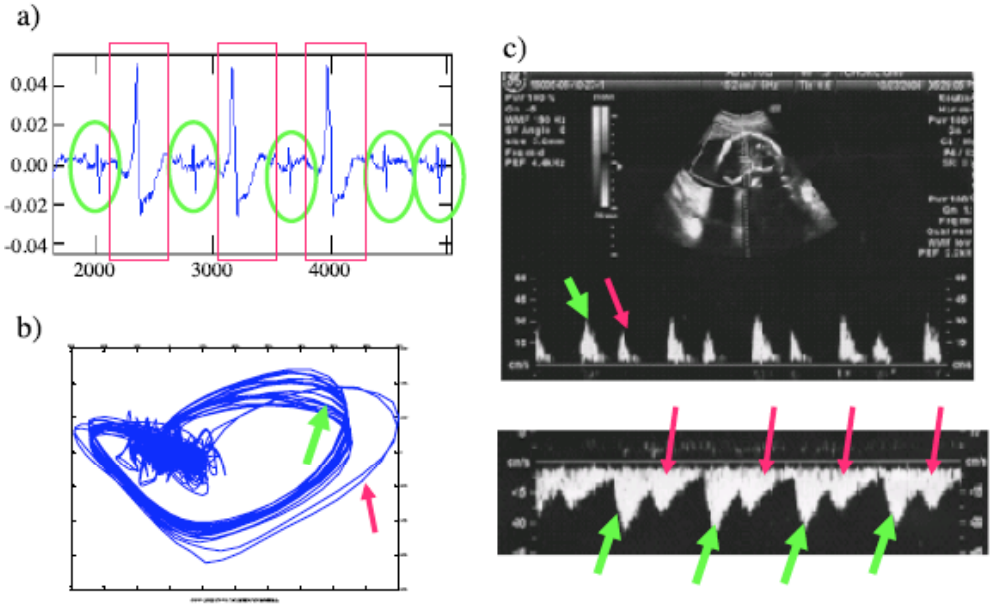

Fig. (2). An example of PVC. PVC is clearly noticed in red squares and normal heart ECG is in green circles in panel **a**). The vector ECG of this case is shown. PVC is clearly noticed in the vector ECG of **b**). In the Doppler velocity waveform of fetal blood flow, it is noticed that a normal ECG (green arrows) corresponds to a normal flow but PVC (red arrows) makes a weak blood flow in **c**).

difficult to diagnose complete atrioventricular block (AV block). The latter requires continuous Doppler signals from the fetal heart because P waves are sometimes too small to detect without references.

The example of PVC is shown in Fig. (**2**). PVC is clearly noticeable in the red squares and normal heart ECG is in the green circles. In the Doppler velocity waveform of fetal blood flow, a normal ECG corresponds to a normal flow but a PVC would correspond to a weak blood flow. The vector ECG of this case is shown. PVC is clearly noticed in the vector ECG. This PVC appeared at 24 weeks gestation, and continued throughout the pregnancy. In the fetal outcome, atrioventricular septal defect (AVSD) was noted. Arrhythmia such as PVC in this case as observed throughout pregnancy may be a marker for a congenital heart defect [5]. Meanwhile, a transient case of arrhythmia is usually functional arrhythmia caused by physiological phenomena such as hyper-activation of ion channels in the fetal myocardial cell.

Furthermore, ectopic beats once thought to be entirely benign, are now recognized to have an important pathologic association [6]. For this, fetal ECG would be an ideal method for diagnosis, but the detection of P and T waves still need averaging over a number of cardiac cycles, which ultimately restricts its usage in this type of fetal arrhythmia detection. We are currently developing a new method for the diagnosis of ectopic heart beats by using fetal ECG with continuous Doppler signals [5, 7].

3.3. Fetal ECG Waveform

It is well known that many factors can affect the fetal ECG waveform. Hypoxia, ion channel activity of myocardial cells, autonomic nervous activity and congenital heart defects account for the majority of cases. When using the BSS method, fetal position relative to the electrodes strongly affects the fetal ECG waveform. On the other hand, with BSSR this phenomena is less observable [3].

In hypoxia, it is well known that the ST segment of ECG waveform changes. The change can be explained by differences in myocardial excitation between the inner and outer layers of the heart. In an adult heart, ST depression of the ECG waveform is explained by local hypoxia at the outer layer caused by decreasing amounts of blood flow to this area. But in the fetal heart, hypoxia occurs in throughout the whole body, so therefore, both layers are ischemic at the same time. Thus, ST depression is hard to be explained by their difference. Moreover, we can observe ST depression during fetal asphyxia in both animal models and clinical cases (Fig. **3**). From these it has been observed that there exist different patterns of behavior of ion channels in fetal myocardial cells [8]. Further investigation is warranted to ascertain the mechanism of T waveform change based on the inherent properties of these fetal myocardial cells.

3.4. Accuracy of Fetal ECG *Via* the Maternal Abdominal Wall

To investigate the accuracy of fetal ECG in our study, we compared it to scalp electrode fetal ECG in the 1st stage of labor. The null hypothesis was that there would be a difference between fetal ECG and scalp electrode fetal ECG. Data from 2 pregnant women with singleton pregnancies of 38- and 41-weeks of gestation were analyzed. The patients were enrolled in the study after written and informed consent were obtained. The correlation coefficient and Bland-Altman plot were calculated to evaluate the coincidence of these two methods (Fig. **4**). Fetal heart rate variability from both fetal ECG were coincident and a linear relationship between the two methods was confirmed. The total average correlation coefficient was 0.998 (n=491). The Bland-Altman plots showed a small bias of 0.51 bpm which was significant. The minimum and maximum values of for the limits of agreement were -0.51 bpm and +0.51 bpm respectively. Ninety five percent of the intervals were noted to lie within ±1bpm.

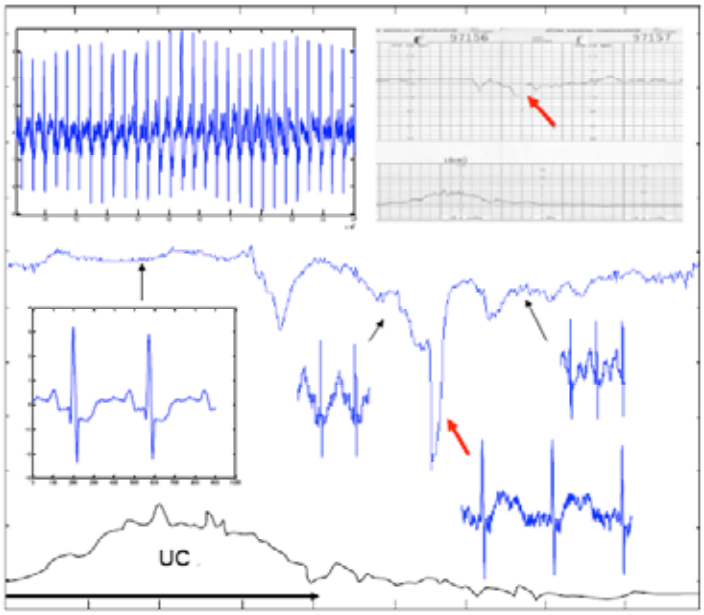

Fig. (3). An example of a fetal ECG waveform during hypoxia. Left upper panel shows an 11 seconds trend of fetal ECG during uterine contractions (UC). The right upper panel shows the fetal cardiotocogram during a late deceleration. The late deceleration occurred with a uterine contraction. The middle big panel shows an instantaneous heart rate tracing pattern of this deceleration calculated from the fetal electrocardiogram. The red arrow in this panel indicates an abrupt drop of fetal heart rate. Such sudden drops could not be detected in traditional Doppler cardiotocograms (red arrow in right upper panel). The left middle small panel shows the averaged fetal electrocardiogram waveforms. ST depressions were clearly noticed. The ST depressions were noted to disappear and the ST elevations were noticed during deceleration.

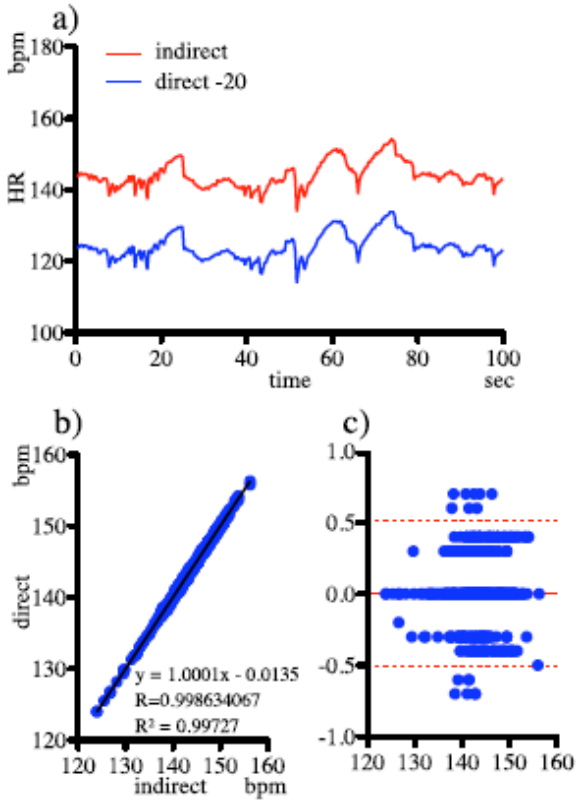

Fig. (4). Accuracy of fetal ECG via the maternal abdominal wall. **a**) The red graph shows an instantaneous heart rate tracing pattern of a deceleration calculated from the fetal ECG via the maternal abdomen (indirect). Blue graph shows an instantaneous heart rate tracing pattern of the deceleration pattern calculated from the scalp electrode fetal ECG (direct). Both heart rates are almost completely coincident. **b**) shows a linear correlation between the two heart rates. The correlation coefficient was 0.9986. **c**) shows the Bland-Altman plots where a small bias of 0.51 bpm was significant. The minimum value for the limits of agreement was -0.51 bpm and the maximum was +0.51 bpm wherein 95% intervals of the points lie within±1bpm.

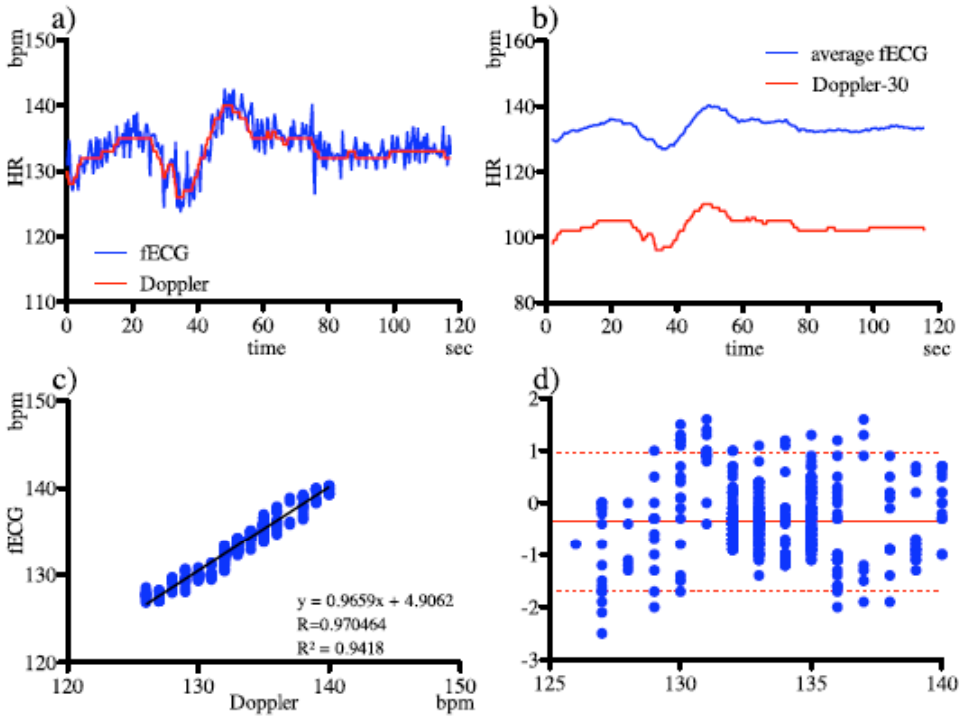

Fig. (5). Accuracy of traditional Doppler cardiotocography. **a**) is one example of comparison between fetal heart rate from fetal ECG (fECG, blue line) and fatal heart rate from traditional Doppler CTG (Doppler, red line) in a singleton fetus at 24 weeks of gestation. The former clearly had more short term variability (STV) than the latter. **b**) The blue line shows the moving average of fECG over each of the 15 time points (3.75sec) (average fECG). The red line represents the Doppler-30bpm line. **c**) shows a linear relationship between the two data. The correlation coefficient was 0.970. **d**) are the Bland-Altman plots which show a significant small bias of 1.3 bpm. The minimum value for the limits of agreement was -1.6 bpm and the maximum was +1.0 bpm wherein 95% intervals of the points lie within±5bpm.

These small differences seemed to arise from the differences between the fetal ECG waveform of each method.

3.5. Accuracy of Traditional Doppler Cardiotocography

To study the difference between fetal ECG and traditional Doppler cardiotocography (CTG), we compared the calculated fetal heart rates of the two methods. The correlation coefficient and Bland-Altman plots were used to evaluate their coincidence. Data from 10 pregnant women with singleton pregnancies from 24- to 38-weeks gestation were analyzed. All patients were entered into the study after written and informed consent was obtained (Fig. **5**).

Fetal heart rate from fetal ECG clearly had more short term variability (STV) than fetal heart rate from traditional Doppler CTG. After a 0.25 sec re-sampling, the moving data was averaged over 15 time points (3.75sec) to confirm equivalence reliability. A linear relationship between the two methods was noticed. The total average correlation coefficient was 0.92±0.09 (n=4,206). The Bland-Altman plots showed a small but significant bias of 3.0 bpm. The minimum and the maximum values for the limits of agreement were -2.57 bpm and +3.38 bpm respectively. Ninety five percent of the intervals were noted to lay within±5 bpm which was coincidentally the traditional accuracy of Doppler CTG.

The Bland-Altman plot in Fig. (**4**) shows the constant difference between the heart rate type and that of Fig. (**5**) shows the constant average of the heart rate types. The Bland-Altman patterns of these two figures were different. The underlying significance of these results may be found in the difference between the two methods. The scatter of the points in Fig. (**4**) appeared a minute diversion from the normal distribution while the structural distribution of points in Fig. (**5**) was possibly representative of an association between fetal ECG and fetal heart movement. Nevertheless, the differences between the two signals were within the permissible ranges in each plot.

In our study observations, heart rate variability of less than 0.267 Hz (=1/3.75) by Doppler CTG was considered reliable, but over 0.267 Hz data was dubitable.

STV was noticeable from 24 weeks gestation with its distribution in fetal heart rate tracings observably changing from random to structural forms all throughout gestation. Fetal heart rate variability has been regarded as an important parameter in the assessment of fetal states. In our previous experiments with fetal lambs, STV was reduced by parasympathetic blockade. This result demonstrated the association between fetal autonomic activity and changes in fetal heart rate STV [9]. In more recent studies, parasympathetic nerve activity significantly prevented fetal brain damage under hypoxic conditions [10]. From this point of view, fetal STV analysis by using fetal ECG measurement will open a new paradigm for the next generation of fetal monitoring systems.

The necessary groundwork for stable measurement of fetal ECG has been established. We hope to make further progress in the future based on these foundations.

CONFLICT OF INTEREST

None declared.

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