Non-Invasive Uterine Electromyography in High BMI Laboring Patients

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Research Question

Is non-invasive uterine electromyography, specifically for high BMI labor patients' contractions, accurate against existing sensors (TOCO and IUPC)?

Background

Non-invasive uterine electromyography is an alternate way to record contractions in laboring patients, using electrical activity in the uterine muscle. Most notably, it is non-invasive and does not need to be readjusted once placed.[2] Contraction output from the tocodynamometer significantly deteriorates as the patients' BMI becomes higher. Intrauterine pressure catheter, while the gold standard, requires rupture of membranes and therefore, is a higher risk of infection. Even in cases of high BMI, the contraction accuracy from uterine electromyography remains high.

Methods

156 laboring, term patients from SSH's BU and MSC units were monitored with MindChild's Meridian M110 device and either the tocodynamometer or intrauterine pressure catheter (TOCO or IUPC) simultaneously. True positive, false positive, and false negative contractions were recorded against the contraction method used by the labor management team (TOCO or IUPC). Sensitivity and positive predictive value of contractions were calculated using statistical formulas.

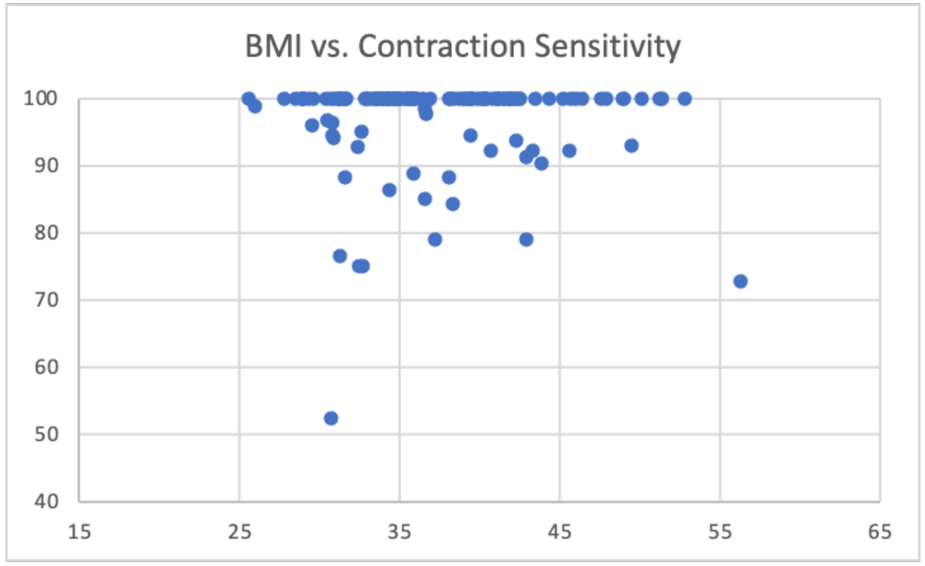
$$\text{Sensitivity: } \frac{TP}{TP+FN}$$

$$\text{Positive Predictive Value: } \frac{TP}{TP+FP}$$

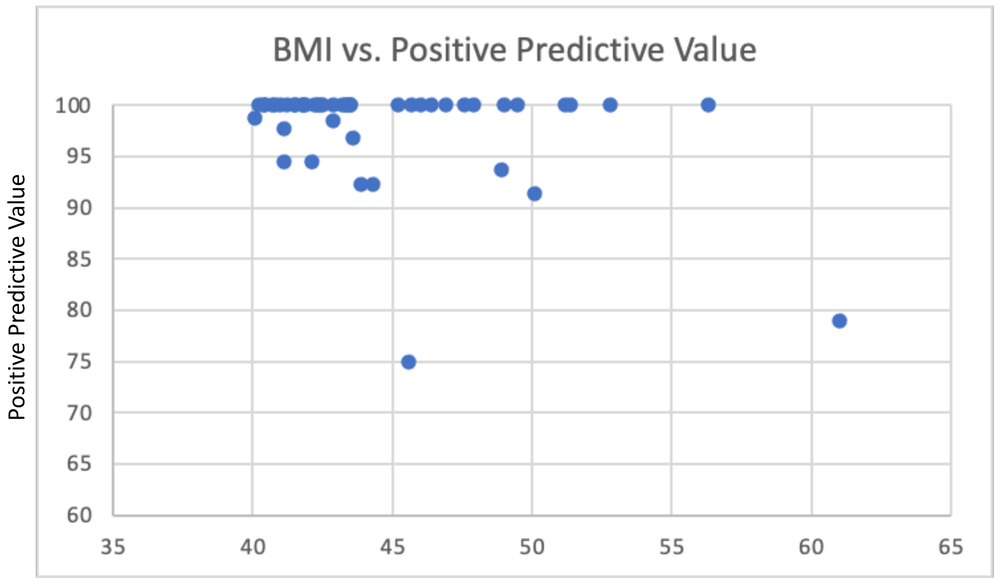
True Positive=TP
False Negative=FN
False Positive=FP

Results

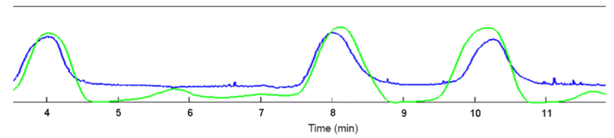
- The sensitivity of the uterine EMG in the study participants from the Meridian M110 was calculated to be 96.4129 overall.
- The positive predictive value was 93.3972.



- As BMI increases, the contraction sensitivity and positive predictive value remains relatively constant, with few outliers throughout the BMI spectrum.
- 48 patients with a BMI of 40 or higher had a contraction sensitivity rate of 96.084%, while the positive predictive value was 90.716.



Results cont.



Visual example of simultaneous contraction monitoring with existing sensors vs. Meridian M110[3]

- Meridian M110 in green
- IUPC in blue

Discussion/Recommendations

The use of non-invasive uterine EMG is a useful and accurate tool to use for laboring patients, especially those of higher BMI, where the TOCO or IUPC is not feasible. Members of the labor management team must constantly readjust the TOCO, taking time away from other nursing and patient care activities. In addition, the placement of the IUPC requires rupture of membranes and increases risk of infection.[4] It also requires advanced first stage of labor. Uterine EMG performs well against the existing hardware, as shown by the high sensitivity rate and positive predictive value, especially in patients with a BMI of 40 and above. This tool can be used by the labor management team for increased patient comfort and reduced adjustment time for high BMI labor patients. This can potentially decrease the number of birth complications and unnecessary cesarean sections, improving birth outcomes for mother and baby.

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Conflict of Interest Declaration

COI Declaration: Adam Wolfberg, Jay Ward, and Jim Robertson own equity in and are officers in MindChild Medical, Inc,: the sponsor of the study

Evaluation of the fetal QT interval using non-invasive fetal ECG technology

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Evaluation of the fetal QT interval using non-invasive fetal ECG technology

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Abstract

Non-invasive fetal electrocardiography (NI-FECG) is a promising alternative continuous fetal monitoring method that has the potential to allow morphological analysis of the FECG. However, there are a number of challenges associated with the evaluation of morphological parameters from the NI-FECG, including low signal to noise ratio of the NI-FECG and methodological challenges for getting reference annotations and evaluating the accuracy of segmentation algorithms. This work aims to validate the measurement of the fetal QT interval in term laboring women using a NI-FECG electrocardiogram monitor. Fetal electrocardiogram data were recorded from 22 laboring women at term using the NI-FECG and an invasive fetal scalp electrode simultaneously. A total of 105 one-minute epochs were selected for analysis. Three pediatric electrophysiologists independently annotated individual waveforms and averaged waveforms from each epoch. The intervals measured on the averaged cycles taken from the NI-FECG and the fetal scalp electrode showed a close agreement; the root mean square error between all corresponding averaged NI-FECG and fetal scalp electrode beats

was 13.6 ms, which is lower than the lowest adult root mean square error of 16.1 ms observed in related adult QT studies. These results provide evidence that NI-FECG technology enables accurate extraction of the fetal QT interval.

Keywords: non-invasive FECG, ECG morphological analysis, crowd-sourcing, medical annotations

(Some figures may appear in colour only in the online journal)

Introduction

Continuous fetal heart rate monitoring is the standard of care for intrapartum management in the United States and in many other countries (American College of Obstetricians and Gynecologists 2005). The limitations of this technology—particularly the very low specificity—are well known, along with the association between the use of continuous fetal heart rate monitoring and an increase in operative vaginal deliveries and cesareans (American College of Obstetricians and Gynecologists 2005). Obstetricians, however, have few alternatives due to the difficulty in monitoring other physiologic signals from the fetus during pregnancy and labor.

The one fetal signal that has generated the most interest is the fetal ECG waveform, which can be reliably obtained during labor with the use of an invasive fetal scalp electrode (FSE), and less reliably using non-invasive adhesive electrodes attached to the maternal abdomen (Wolfberg and Norwitz 2009, Sameni and Clifford 2010, Behar *et al* 2016).

Most studied is the ratio between the *T*-wave and the *R*-wave, a metric analyzed and reported by the STAN monitor (Neoventa Medical, Goteborg, Sweden) as a proxy for the ST segment. There is a reasonable physiologic basis for monitoring the ST segment during labor as a marker for hypoxia or ischemia (Greene 1987, Greene and Rosen 1989). Although a large American study failed to find improved newborn outcomes or reduced cesarean rates when the STAN monitor was used (Belfort *et al* 2015), multiple independent trials in Europe have demonstrated significant improvements in newborn outcome when the STAN monitor was used (Amer-Wahlin *et al* 2001, Doret *et al* 2011, Kessler *et al* 2013).

Less research has been conducted on the association between the fetal QT interval and newborn outcome, even though many studies link QT-interval abnormalities during the fetal and newborn period with serious events, including sudden infant death syndrome (Crotti *et al* 2013). Oudijk and colleagues used the STAN monitor to measure the QT interval and demonstrated that during severe intrapartum hypoxia and metabolic acidosis, there was a significant shortening of the QT and corrected QT interval (Oudijk *et al* 2004). More recently one group identified a fetus as having long QT syndrome using QT measurement performed on the non-invasive fetal ECG (NI-FECG) (Fujimoto *et al* 2009). In adults, the QT interval has been of high interest in a number of conditions including the Romano–Ward and Jervell–Lange-Neilson syndromes, drug toxicity, and to predict prognosis following acute myocardial infarction (Campbell *et al* 1985).

Other pathologic conditions linked to an abnormal QT interval include an association between a prolonged QT interval in newborns and the use of selective serotonin reuptake inhibitors (SSRI) during pregnancy (Dubnov *et al* 2005, Dubnov-Raz *et al* 2008). These observations suggest the potential to screen for adverse events using the fetal QT interval during pregnancy and labor.

Hampering research is the requirement that a wire electrode be directly attached to the fetal scalp in order to obtain a reliable signal. Placement of the FSE requires ruptured membranes

and a dilated cervix and thus this modality is limited to monitoring during labor. Furthermore, the FSE does not allow for monitoring of the fetus prior to labor, and because the FSE has only one electrode on the fetal scalp, it does not cover the 3D electrical field emanating from the fetal heart. In contrast, the NI-FECG monitor could be used for antepartum (as well as intrapartum) fetal monitoring and it provides a 3D electrical representation of the electrical field emanating from the fetal heart. Thus, there is a strong motivation for developing a non-invasive method for measuring the FECG obtained from multiple abdominal ECG sensors. Indeed, NI-FECG is a non-invasive monitoring method that allows to estimate the FHR, as well as information on the electrical activity of the heart which is embedded in the ECG morphology.

Accurate extraction of the FHR from the NI-FECG has been demonstrated (Behar *et al* 2014, Clifford *et al* 2014). Our group previously has described the accurate measurement of the ST segment from the external fetal ECG recordings (Clifford *et al* 2011). However, accurate QT interval estimation from NI-FECG has not been previously demonstrated.

To be clinically useful, the fetal QT interval measured using abdominal ECG technology must be reliably identical to the fetal QT interval measured using a direct ECG measurement. We sought to validate the non-invasive measurement of the fetal QT interval in order to allow for additional research to be conducted without the need for a FSE. This paper describes the method for rigorously comparing the fetal QT intervals extracted from the NI-FECG and FSE, and demonstrates the feasibility of fetal QT measurement from the NI-FECG signal.

Materials and methods

The study was approved by the Institutional Review Boards at the institutions where data were collected: Brigham and Women's: 2010-P-00278/1, Cleveland Clinic Fairview: 12–154, Newton Wellesley: N08-445 and Tufts Medical Center: 7863 20. Fetal ECG data were recorded from 22 term laboring women with singleton fetuses. Data were recorded simultaneously using a 28 NI-FECG monitor (Mindchild Medical, North Andover, MA) and a single lead invasive FSE (GE Corometrics). Data were recorded at a sampling frequency of 1 kHz with 16-bit accuracy. All women delivered newborns with five-minute Apgar scores above six, and none of the fetuses were exposed to SSRI medication in-utero. There were no prolonged QT intervals noted by the three independent reviewers of the data or any indications for long QT syndrome from the clinical data.

Each recording period was divided into one-minute segments for the analysis. Segments were selected that had a relatively stable fetal heart rate based on determination that the baseline heart rate did not change by more than 20 bpm during the one-minute period (Silva *et al* 2013). In segments that contained accelerations or decelerations (defined as changes from baseline of more than 20 bpm lasting more than 15 s) the corresponding sub-segments (generally lasting between 10–15 s) were replaced by random noise to ensure the annotators were not annotating in areas with large changes in heart rate. This procedure was implemented to ensure that the fetal QT interval was approximately stable over each one-minute segment, which is necessary when computing averages of ECG cycles (Christov and Simova 2006). Indeed, a relationship between the QT length and the heart rate has been established in adults (Bazett 1920) and although such a relationship has not been studied in fetuses, it is reasonable to assume that the QT length be modulated by the fetal heart rate (even if differently than for adults).

The QT interval is defined as the time interval between the Q wave onset and the end of the T wave in the heart's electrical cycle. Three pediatric cardiologists independently annotated the data using the modified Physionet Lightwave interface (Zhu *et al* 2014) (example in

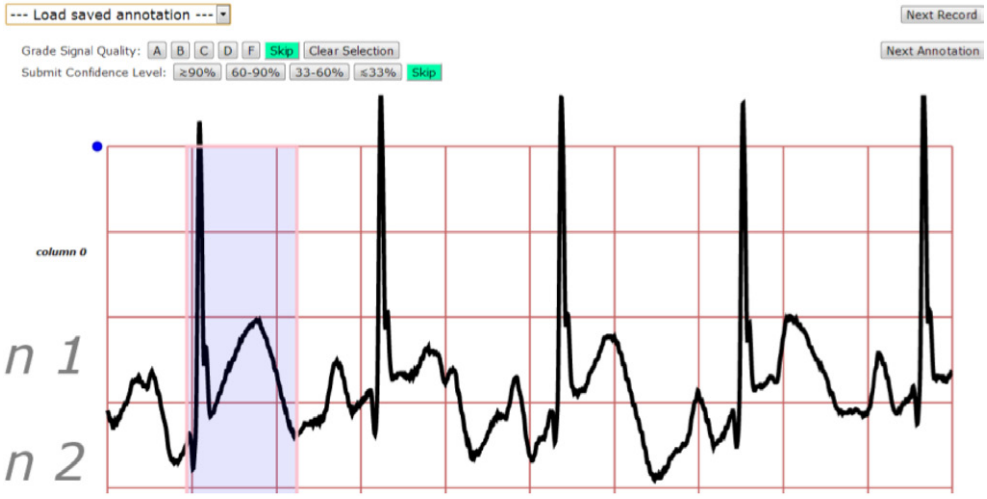

Figure 1. Annotation interface. A fetal QT interval was annotated by dragging a mouse across the interface from left to right (shaded area). The signal in this illustration is a FSE segment. The procedure was also repeated for the ECG derived from the non-invasive FECG.

figure 1). This online system either presented the cardiologists with a rhythm strip one minute long, or presented them with a single ECG waveform created by automatically averaging a series of ECG waveforms. Each cardiologist was trained on the interface individually during an online training session. The precision of the annotation interface was 1 ms.

The first set of annotations, denoted SET1, contained 210 one-minute segments (105 recorded using abdominal electrodes and the corresponding 105 segments recorded using a FSE). Each cardiologist was instructed to annotate five QT intervals per one-minute segment, and was told that they were free to choose the five cycles to annotate, a methodology similar to prior manual QT annotation exercises (Moody *et al* 2006). The next set, denoted SET2, included 210 averaged fetal ECG cycles (105 abdominal and 105 corresponding FSE). One annotation per waveform was requested. Cardiologists were blinded to signal source (i.e. whether the signal to annotate was FSE or NI-FECG) and the waveforms were presented at random.

In each set, the data were randomized so that two consecutive waveforms were not extracted from the same patient. An example of an annotation made on a rhythm strip segment is demonstrated in figure 1. Examples of signals used in SET1-2 are shown in figure 2.

We analyzed the variation between paired measurements of the QT segment (measured on the NI-FECG and FSE). For that purpose the root meant square error (RMSE) and absolute error (AE) were computed. We also evaluated the RMSE95 and AE95 defined as the RMSE and AE evaluated while excluding the extreme 5% values. This was done to make sure that no outliers in the sample size were biasing the estimation of the RMSE and AE. Three methods for fusing the annotations were investigated: mean, median and an expectation maximization (EM) algorithm (Zhu *et al* 2014)—see description in the following paragraph. In addition Wilcoxon signed rank test was applied to test the hypothesis that the difference between scalp and abdominal annotations were samples from continuous distributions with zero median for both SET1 and SET2. The EM algorithm used for fusing the annotations is described in the context of QT annotation in Zhu *et al* (2014). It is assumed that R annotators have annotated a series of N, QT observations. The true QT annotation for each individual record is written

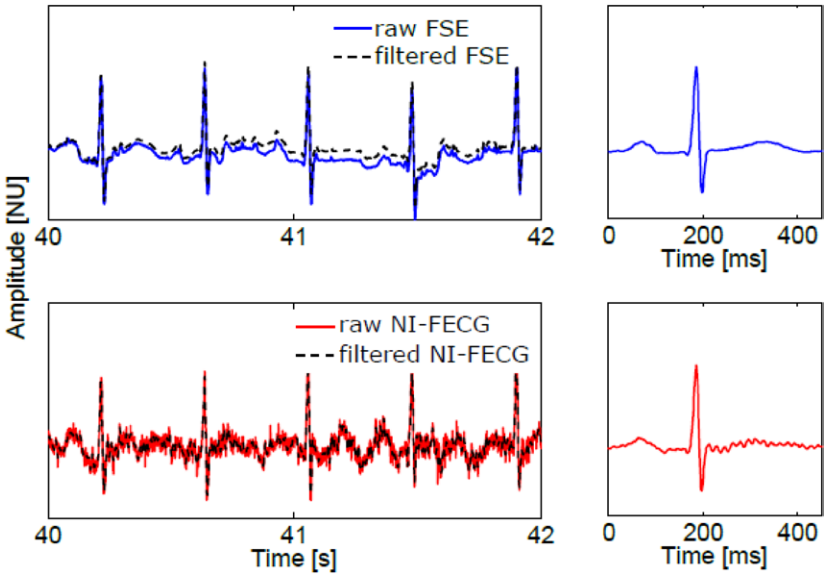

Figure 2. Example of signal used for SET1 and SET2. Top left: raw (solid line) and filtered (dashed) FECG from FSE; Top right: corresponding average ECG; Bottom left: raw (solid line) and filtered (dashed) abdominal NI-ECG; Right: corresponding average ECG templates constructed from the raw ECG signal.

z_i, $i \in [1;N]$ and the annotation from annotator j and which was performed on record i is denoted y_i^j. In addition, it is assumed that z_i can be predicted using a linear regression model: $z_i = \underline{w}^T \cdot \underline{x}_i + \epsilon$, where $\underline{w}$ is the regression vector and ϵ is a zero-mean Gaussian noise with precision γ and $\underline{x}$ is a feature vector. No features were used in the approach detailed here and thus $\underline{x}$ is a unity vector. The EM algorithm can be summarized as follows:

(1) E-step: the E-step estimates the expected true annotations for all records, $\underline{\hat{z}}$, as a weighted sum of the provided annotations with their precision λ^j.

$$\underline{\hat{z}} = \frac{\sum_{j=1}^{R} \lambda^j \cdot \underline{y}^j}{\sum_{j=1}^{R} \lambda^j}$$

(2) The M-step is based on the current estimate of $\underline{\hat{z}}$ and given the dataset written D. The model parameters such as the regression coefficient $\underline{\hat{w}}$ and precision $\underline{\hat{\lambda}}$ can be updated using the following equations:

$$\frac{1}{\hat{\lambda}^j} = \frac{1}{N}\sum_{i=1}^{N}(y_i^j - \underline{\hat{w}}^T \cdot \underline{x_i})^2$$

$$\underline{\hat{w}} = \left(\sum_{i=1}^{N} \underline{x_i} \cdot \underline{x_i}^T\right)^{-1} \sum_{i=1}^{N} \underline{x}_i \cdot \hat{z}_i$$

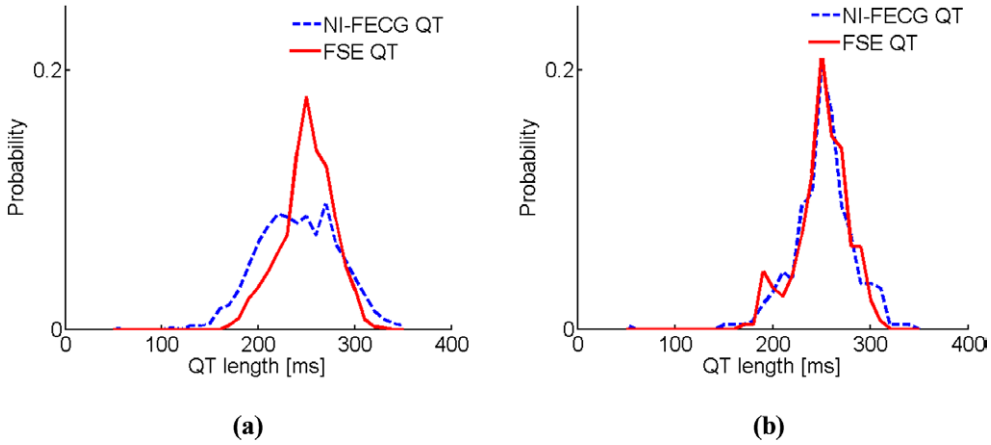

Figure 3. Empirical probability density function for the median FSE QT interval annotated by the three annotators for: (a) SET1 (i.e. annotation on the raw signals), 3150 annotations, and (b) SET2 (annotation on the averaged heart beat cycles) 630 annotations. For SET2, the two distributions (NI-FECG QT and FSE QT) superimpose closely, while the NI-FECG QT distribution has a lower median and is more platykurtic (broader) than the FSE QT distributions for SET1, indicating more extreme values.

With

$$\hat{z}_i = \frac{\sum_{j=1}^{R} y_i^j \lambda^{\mathrm{j}}}{\sum_{j=1}^{R} \lambda^{\mathrm{j}}}$$

The precision is initialized as being equal for all annotators (i.e. at the initial step of the algorithm). The initial precision can thus be written as: $\underline{\hat{z}} = \frac{1}{R}\sum_{j=1}^{R} \underline{y}^j$.

Results

Cycles with high correlation were retained to build the averaged cycles and a minimum of 20 cycles per 1 min segment were required to form a valid template. The QT interval measured using the FSE was 0.3 ms shorter, on average, than the QT interval measured using NI-FECG when averaged cycles were annotated and 8.7 ms longer when individual cycles were annotated. Figure 3 shows the probability density function for the fetal QT interval annotated by the three annotators for SET1 and SET2. On this plot, NI-FECG QT refers to the QT annotated on the NI-FECG extracted using the MindChild monitor and FSE QT refers to the QT annotated on the FSE by the reviewers. For SET2, the two distributions (NI-FECG QT and FSE QT) superimpose almost perfectly (without a significant difference between the distributions), while the NI-FECG QT distribution has a lower median and is more platykurtic (broader) for SET1. For SET1, the null hypothesis of the Wilcoxon signed rank test was rejected under the 5% significance level whereas the null hypothesis could not be rejected for SET2. This statistical test confirms that the distributions for scalp and abdominal annotations only matched (i.e. were not significantly different) when using the averaged cycles of the NI-FECG and FSE.

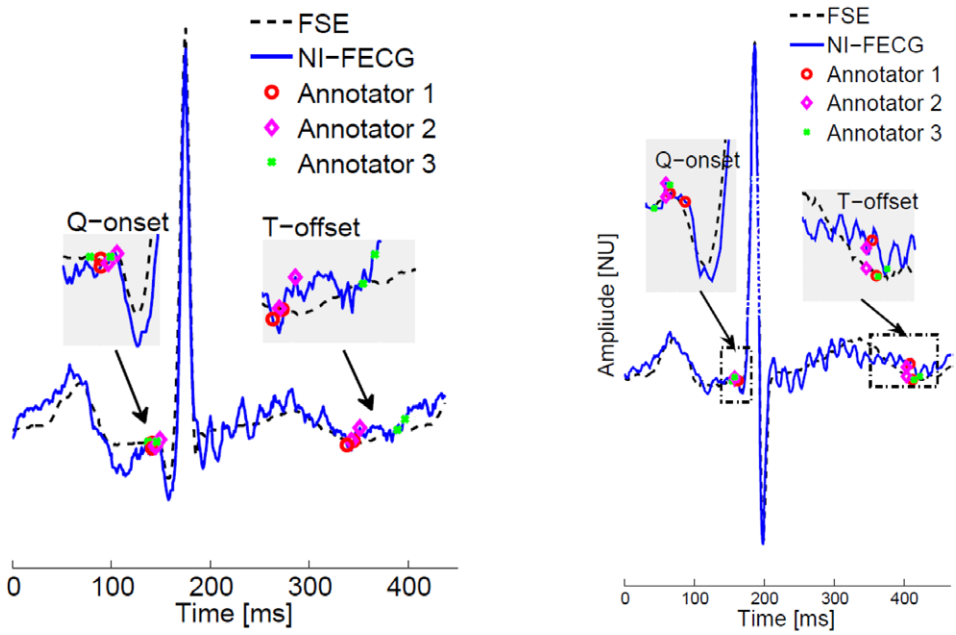

Figure 4. Comparison of annotations performed on average FECG waveforms from both the FSE and the NI-FECG monitor by three experts. (a) Note the close correspondence between experts on both the FSE and NI-FECG signal. (b) Note the disagreement between annotator 3 and the other two experts. This last example illustrates the importance of combining annotators to improve the reliability of results.

Figure 4 shows two examples of averaged cycles (FSE and NI-FECG) being annotated by the three experts. The figure shows the close agreement between the expert annotations on the FSE and on the NI-FECG. A total of 3150 annotations were performed for SET1 (1050 per annotator) and 630 for event 2 (210 per annotator). Tables 1 and 2 presents the results for SET1 and SET2 when considering each individual annotator and all the annotators combined. The AE of 14.2 ms and 10.4 ms for SET1 and SET2 respectively when combining all the annotators compares favorably to AEs reported in the literature when adult data are annotated in a similar fashion.

Figure 5 shows that combining the annotations from the three experts resulted in a lower bias, a slope closer to one and higher goodness of fit ($R^2 = 0.61$) than any of the three annotators taken individually. The intraclass correlation coefficient (ICC) was also computed between each individual annotator annotations on the SQT and AQT to quantify how much the two sets of annotations resembled each other. ICC of 0.522, 0.613, 0.616 for annotators 1–3 were obtained. The relative ranking between the three annotators is in accordance with the χ^2 evaluated (see figure 5).

Discussion and conclusion

This is the first paper to demonstrate that the fetal QT interval can be reliably measured from ECG data recorded non-invasively using electrodes on the maternal abdomen. Although we note that no pathologically long or short QT intervals were present in the data available, we

Table 1. Individual annotators (A1)–(A3) and annotations for SET1 and SET2.

Method/stats	RMSE	AE	RMSE95	AE95
A1-EVENT1	27.5	22.5	25.0	20.7
A2-EVENT1	41.3	32.8	35.9	29.5
A3-EVENT1	21.6	17.1	19.2	15.5
A1-EVENT2	33.2	20.3	22.0	16.3
A2-EVENT2	22.7	16.6	17.8	14.1
A3-EVENT2	18.3	14.8	16.2	13.4

Note: Reference: FSE QT obtained from annotator A. Measure: non-invasive fetal ECG QT obtained from annotator A. RMSE95 and AE95: RMSE and AE when removing the 5% extreme values. All values are expressed in ms. The lowest AE is underlined and also corresponds to the lowest RMSE.

Table 2. Combining cardiologists' annotations to get FSE QT and non-invasive fetal ECG QT for SET1 and SET2.

Method/stats	RMSE	AE	RMSE95	AE95
Mean-EVENT1	17.9	14.1	15.1	12.4
Median-EVENT1	21.3	17.1	18.7	15.5
EM-EVENT1	18.0	14.2	15.3	12.7
Mean-EVENT2	15.4	11.5	12.1	9.9
Median-EVENT2	18.8	14.2	15.8	12.5
EM-EVENT2	13.6	10.4	11.4	9.2

Note: The error is assessed for the mean/median/EM non-invasive fetal ECG QT against mean/median/EM FSE QT approaches for fusing the annotations. RMSE95 and AE95: RMSE and AE when removing the 5% extreme values. All values are expressed in ms. The lowest AE is underlined and also corresponds to the lowest RMSE.

do not see any significant reason to believe the signal processing of our FECG would lead to significant distortions, since we have shown in earlier work that low frequency components of the FECG are not distorted by our extraction process (Clifford *et al* 2011). However, definitely proving this remains a topic for future studies with a significant prevalence of fetuses with short or long QT intervals.

Our annotators, who were blinded to the source of the waveform they were annotating, generated QT intervals with excellent correlation between abdominal data and corresponding FSE signal when averaged waveforms were used. In contrast, when individual waveforms were annotated, the distortion inherent to the waveforms led the annotators to generally identify shorter QT intervals when annotating the abdominal signals than the FSE signals (see figure 3). These findings, suggest that the most accurate approach to fetal QT annotation will be to use a waveform created from a running average of several heartbeats. This was confirmed by the quantitative analysis presented in tables 1 and 2 where the results for the experiment on SET2 were consistently better. Combining the annotations from the three electrophysiologists resulted in a lowering of the RMSE (from 18.3 ms to 13.6 ms, SET2) and AE (14.8 ms to 10.4 ms, SET2) compared to using any individual annotator. This is in accordance with the finding of Zhu *et al* (2014) for adult QT annotation aggregation. In the case of the experiment on SET2 the expectation maximization algorithm gave the best results.

The magnitude of the fetal QT estimation error obtained in this study (17.9 ms RMSE for SET1 and 13.6 ms RMSE for SET2) compare to the RMSE obtained when combining QT

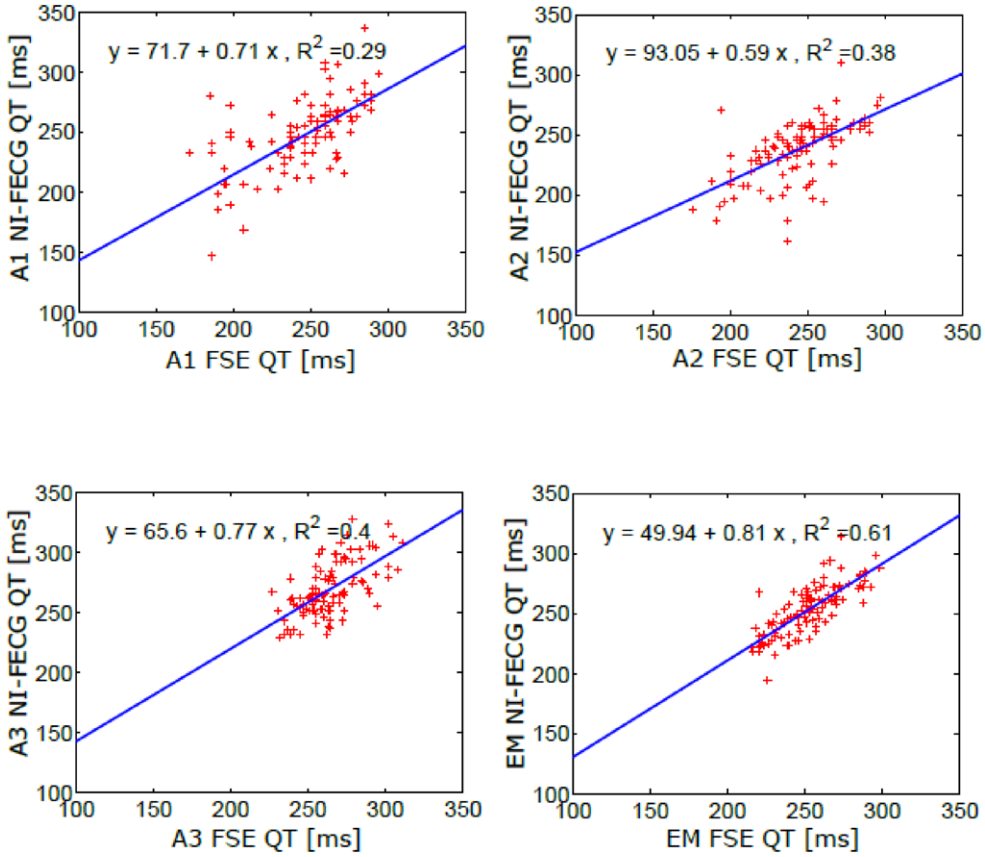

Figure 5. Plot of QT annotations from the extracted NI-FECG obtained using the NI-FECG monitor (denoted NI-FECG QT) against QT annotations from the FSE signal (denoted FSE QT), 22 fetuses (105, 1 min segments). A: annotator. (e.g. A1 NI-FECG QT refers to the QT annotated by annotator one on the NI-FEGC output from by the Meridian monitor). EM: crowd sourced annotations from the three clinicians using the EM algorithm (e.g. EM FSE QT refers to the scalp QT annotations merged using the EM algorithm). Line fit is given by: $y =$ intercept $+$ gradient x, R^2 is the corresponding coefficient of determination (goodness of fit).

annotations from three annotators on adult ECG (RMSE of 16.07 ms found previously) (Zhu *et al* 2014).

A number of published studies have attempted to extract the fetal QT (and other ECG morphology based quantities) from the NI-FECG or fetal magnetocardiography (Brambati and Pardi 1980, Abboud *et al* 1990, Stinstra *et al* 2002, Taylor *et al* 2005). However, these studies did not validate their measurements with invasive data and thus they did not prove that the algorithms that they used for NI-FECG extraction did not distort the QT length, for example, through the distortion of the *T*-wave by heavy preprocessing of the abdominal data or by moving to the source domain using a blind source separation algorithm (Andreotti *et al* 2016).

Stinstra *et al* (2002) used fetal magnetocardiography (MFCG) recordings from 582 healthy patients at different stages of the pregnancy (gestational age 17–41 weeks) and manually annotated the PR, PQ, QRS and QT intervals, averaging over 100 cardiac cycles per recording.

The QT length was found to be in the interval [149–339] ms ($n = 412$, 16–42 weeks of gestation), but the authors did not have FSE data to validate their measurements. Brambati and Pardi (1980), used NI-FECG to record 421 pregnant women (17–41 weeks) performed a similar set of measurements, averaging 50 cardiac cycles per measurement, again without simultaneous measurement of invasive FECG data. Two other papers performed similar analyses and found the QT to range from 207–338 ms ($n = 21$, 32–41 weeks of gestation) (Abboud *et al* 1990) and 233–329 ms ($n = 11$, 24–41 weeks of gestation) (Taylor *et al* 2005). Although these studies did not validate their measurements with invasive data, the ranges found were similar to the ranges obtained in this paper (see figure 3).

It bears mentioning, however, that there is no gold standard for the fetal QT interval, given the inability to adhere standard electrodes to the fetal precordium. Validation using the FSE is a reasonable approach, however it would be useful to validate the fetal QT interval with ECG data measured immediately after birth. Such data would also provide information on whether the QT interval changes at delivery. Despite the fact that one of the principal advantages of the NI-FECG is its ability to perform antenatal monitoring, the study focused on measurements performed at birth. This is because this is the only alternative for obtaining a QT reference by using the FSE (other than using magnetocardiography, which is expensive and would prohibit the use of the NI-FECG monitor). However, it is important to mention that the accuracy in estimating the FQT from the NI-FECG will likely be lower if the gestational age was significantly lower, since the fetal heart would be smaller and the NI-FECG signal to noise ratio may therefore be lower.

Since the extraction and study of morphological parameters from the NI-FECG is a nascent field, it is difficult to say whether the error reported in this study is low enough to be considered acceptable for fetal QT monitoring. However, it is less than that quoted for adult ECG studies and thus demonstrates a promising application. In addition, it is important to note that recent attempts at estimating fetal QT automatically have provided a root mean square error of over 152 ms, which indicates that our approach provides significant improvements (an order of magnitude reduction in errors) (Silva *et al* 2013, Clifford *et al* 2014).

Similar to prior studies (Silva *et al* 2013), we determined that the QT interval can be most accurately measured by averaging a series of cardiac cycles. Averaging allows the production of quality ECG average cycles by reducing the signal to noise ratio by up to a factor $\sqrt{N}$ (where N is the number of cycles averaged) under certain hypotheses (Rompelman and Ros 1986a, 1986b). However this raises the question of how much `averaging' should be allowed given that the ECG is a non-stationary signal. This question needs further investigation, together with the number of annotators and their associated skill levels needed to create an exact QT estimate (Zhu *et al* 2014).

Despite its relatively small sample size, our study is unique in that we validated the non-invasive fetal ECG QT measurement for each subject against invasive data that is largely absent of potential artifact or error due to the automated extraction process, which is scientifically repeatable. In addition we presented a rigorous protocol for obtaining the fetal QT measurements using an online annotation interface designed by our group and by combining the medical annotations from three expert cardiologists.

Acknowledgment

JB was supported by MindChild Medical Inc. North Andover, MA, by the UK Engineering and Physical Sciences Research Council, the Balliol French Anderson Scholarship Fund, and by the Technion Aly Kaufman Fellowship.

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Evaluation of the fetal T/R ratio using a fetal scalp electrode and abdominal sensors

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Jim Robertson,[3] Adam Wolfberg, MD, MPH,[3,4] Gari Clifford, PhD,[1,3]
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MindChild Medical, Inc.,[3] North Andover, Massachusetts; Tufts Medical Center,[4] Boston, Massachusetts.

Background

Evaluation of the T/R ratio - the metric used by the STAN™ monitor - improves the accuracy of intra-partum fetal assessment when combined with fetal heart rate monitoring, but typically requires a fetal scalp electrode (FSE). Non-invasive measurement of the T/R ratio would make this metric more widely available.

Objective

To compare fetal T/R ratio measured using sensors on the maternal abdomen to the fetal T/R ratio acquired using a FSE.

Methods

Data were acquired from 27 term laboring women who had a FSE placed for a clinical indication. 31 channels of abdominal data were recorded simultaneously with the FSE.

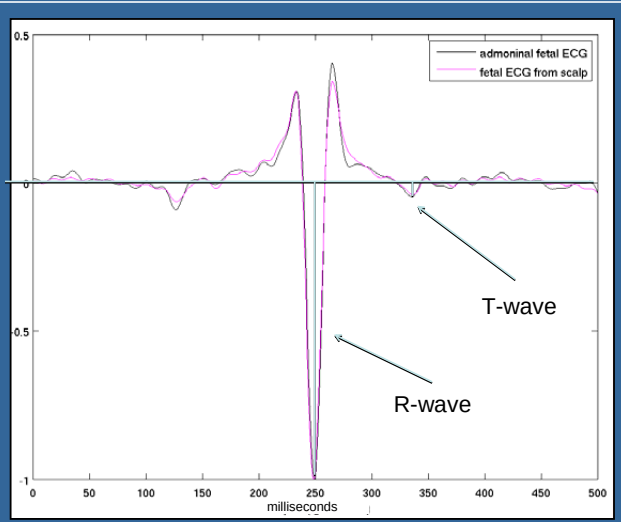


Fig. 1. Comparison of ECG waveform from the FSE and abdominal sensors. The T- and R-waves are illustrated.

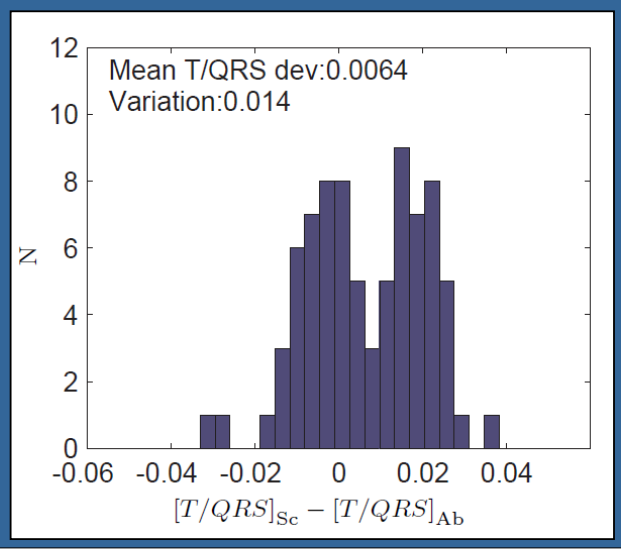


Fig. 2. Variation in T/R ratio between FSE and abdominal sensors.

Methods (cont.)

The average T/R ratio level was estimated from 79 30-second segments from the FSE and the abdominal data for 4 subjects. A comparison was performed to assess the correlation between the fetal T/R ratio derived from abdominal sensors and T/R ratio measured using the FSE.

Results

The difference between the T/R ratio calculated from the scalp electrode and the T/R ratio calculated from the extracted abdominal fetal ECG was 0.0064 ± 0.014. This difference is not clinically meaningful.

Conclusion

We measured the fetal T/R ratio was accurately measured using abdominal electrodes in non-ischemic fetuses.

Comparing the Fetal ST Segment Acquired Using a Fetal Scalp Electrode and Abdominal Electrodes

Gari Clifford, PhD,[1,2,3] Reza Sameni, PhD,[2,4] Jay Ward,[2] Jim Robertson,[2] Courtenay Pettigrew,[5] Adam J. Wolfberg, MD, MPH,[2,5,6]

[1]Oxford University, [2]MindChild Medical, Inc., [3]Massachusetts Institute of Technology, [4]Shiraz University, [5]Tufts Medical Center, [6]Children's Hospital Boston,

Objective:

To compare fetal ST-segment deviation measured using sensors on the maternal abdomen to the fetal ST-segment deviation acquired using a fetal scalp electrode (FSE).

Methods:

Data were acquired from 27 term laboring women who had a FSE placed for a clinical indication. 29 channels of abdominal data and one precordial channel were recorded simultaneously with the FSE. The data were preprocessed for removal of interference from maternal ECG as well as power-line contamination and other sources of background noise, such as muscle artifact.

The median ST level was estimated from 79 10-second segments from the FSE and the abdominal data.

Methods (cont.):

A statistical comparison was performed to assess the accuracy of the ST-segment deviation (elevation or depression) derived from abdominal sensors compared to the FSE.

IRB approval and informed consent were obtained.

Results:

ST elevation from the isoelectric point ranged from 0-2% of R-wave amplitude. ST depression ranged from 0-1.5% of R-wave amplitude. The root mean square error between the ST deviation calculated by both methods averaged over all processed segments was 0.52 percent, and the mean absolute difference was 0.29 percent.

Conclusions:

ST deviation calculated from ECG acquired from the maternal abdomen is clinically indistinguishable from ST-segment deviation measured using the fetal scalp electrode.

Fig. 1. Comparison of ECG waveform from the FSE and abdominal sensors.

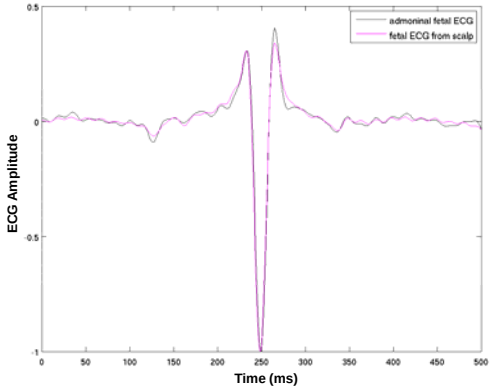
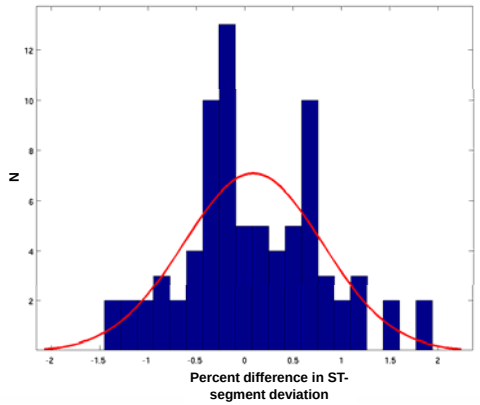


Fig. 2. Distribution of difference in ST elevation between FSE and abdominal sensors.



Disclosure: The authors, except for Ms. Pettigrew, hold equity in MindChild Medical, Inc., which has licensed intellectual property used to generate results presented in this abstract.

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Accuracy of Fetal Heart Rate Acquired from Sensors on the Maternal Abdomen Compared to a Fetal Scalp Electrode

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Objective:

To compare fetal heart rate measured using electrodes on the maternal abdomen to the fetal heart rate acquired using the fetal scalp electrode (FSE).

Methods:

Data were acquired from 27 term laboring women who had a FSE placed for a clinical indication. 29 channels of abdominal data and one chest lead were recorded simultaneously with the FSE. The data were preprocessed for removal of interference from maternal ECG as well as power-line contamination and other sources of background noise, such as muscle artifact.

Methods (cont.):

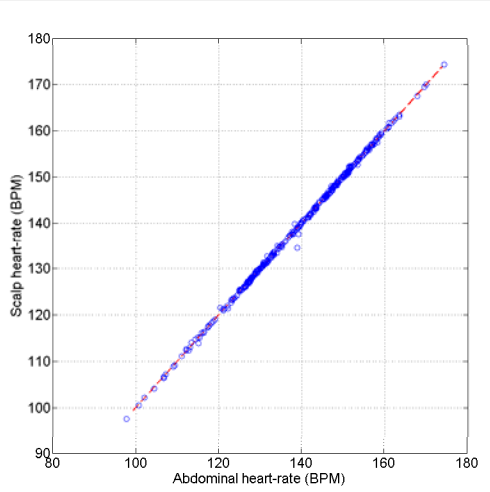
Signal quality measures were used to select regions of usable data from both the scalp and abdominal electrodes. A total of 542 10-second segments, sampled every 30 seconds, were chosen from the FSE and the preprocessed abdominal data.

The associated median fetal heart rate was calculated in each segment of the abdominal and scalp data. A statistical comparison between the fetal heart rate calculated in simultaneous segments of abdominal and scalp data was performed. This allowed us to assess the accuracy of the fetal heart rate recorded from abdominal sensors compared to the "gold standard," FSE.

IRB approval and informed consent were obtained.

Results:

The fetal heart rate was successfully extracted from the FSE from 85.6 percent of analyzed segments, and 83.3 percent of analyzed segments recorded using abdominal sensors.



Results (cont.):

The root mean square error between the fetal heart rate sequence calculated by both methods averaged over all processed segments was 0.35 beat per minute.

Conclusions:

FHR acquired from the maternal abdomen is highly accurate and on average is clinically indistinguishable from FHR calculated from fetal scalp electrode data. Furthermore, using our method, abdominal fetal ECG is useful for FHR estimation almost as often as data from scalp electrode data. Our method can be used as a reliable alternative to the FSE for automated FHR reporting and noisy data rejection.

Disclosure: The authors, except for Ms. Pettigrew, hold equity in MindChild Medical, Inc., which has licensed intellectual property used to generate results presented in this abstract.

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Association of Morphologic Entropy in Fetal ECG with Inflammatory Cytokines and Markers of Neuronal Injury

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Objective:

To evaluate the use of fetal ECG entropy to predict fetal inflammation.

Methods:

Fetal EKG data were recorded during labor using a GE Corometric 120® fetal monitor from six women who had a scalp electrode placed for a clinical indication at term. We measured the morphologic entropy of the fetal ECG signal using an unsupervised algorithm.

The algorithm first partitioned heart beats into classes of activity based on their morphology, and then computed the entropy of the symbolic sequence obtained by replacing each beat in the original signal with a label corresponding to its morphologic class.

Methods (cont.):

Interleukin-6 (IL-6), IL-8, and neuron-specific enolase (NSE) levels were measured in the umbilical cord serum.

Results:

Morphologic entropy showed a statistically significant linear association ($p<0.05$) with IL-6, IL-8, and NSE levels.

There was no association observed between heart-rate variability and any of the measured serum levels.

Conclusions:

Morphologic entropy of the fetal ECG signal may provide a noninvasive means to detect inflammation prior to the development of chorioamnionitis.

Fig. 1. Association between morphologic entropy and IL-6 levels in cord serum (p=0.019).

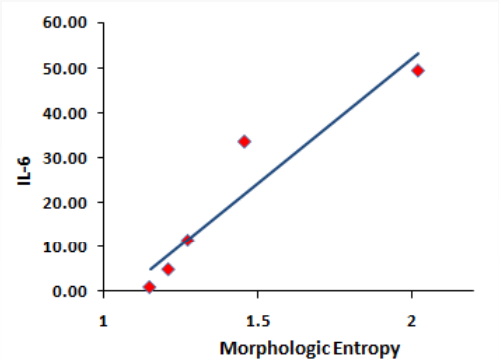


Fig. 2. Association between morphologic entropy and IL-8 levels in cord serum (p=0.009).

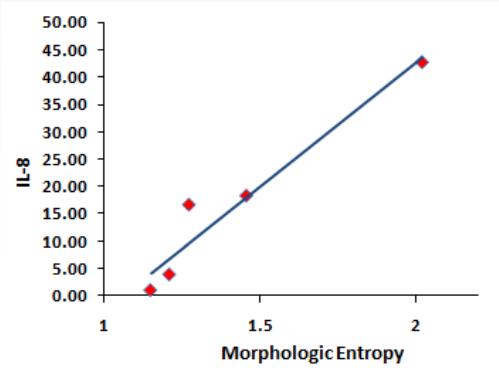
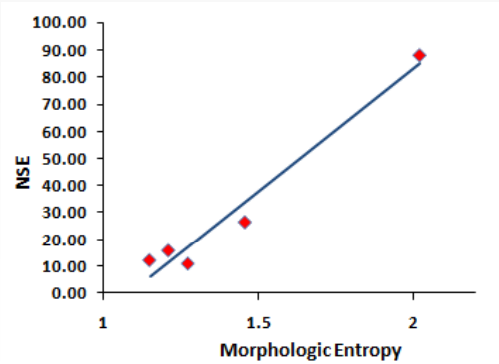


Fig. 3. Association between morphologic entropy and NSE levels in cord serum(p=0.005).



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Development of a Fetal ECG Device – MindChild Medical, Inc.

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MindChild Medical

Jim Robertson, CEO. Jim is also CEO of E-TROLZ Inc. Jim has 30 years experience in industrial automation, design services, and medical device development.

Adam Wolfberg, CMO. Adam is an assistant professor of Maternal-Fetal Medicine at Tufts and a Research Fellow in neurology at Children's Hospital Boston.

Jay Ward, EVP. Jay is also EVP of E-TROLZ. Jay has 26 years of experience in industrial automation and medical device development.

Gari Clifford, CTO. Gari is an associate professor of biomedical engineering at Oxford, and a research affiliate at MIT.

Reza Sameni. Reza is an assistant professor of computer science at Shiraz University.

MindChild's Partners

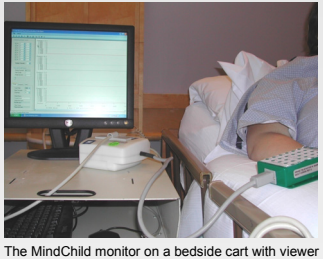
E-TROLZ is an equity partner in MindChild and licenses IP to MindChild. E-TROLZ provides the signal acquisition and digital signal processing platform for the device.

Tufts Medical Center is an equity partner in MindChild and licenses IP to MindChild. Tufts leads IP licensing, and serves as MindChild's primary clinical home.

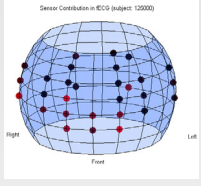
MIT licenses IP to MindChild and collaborates with MindChild on research and data analysis.

Orbital Research, Inc. collaborates with MindChild on development of sensor technology. Orbital receives funding from NICHD to support this work.

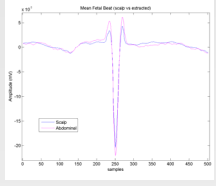
Zeeshan Syed, an assistant professor of computer science at University of Michigan, has a research focus on analysis of ECG signal and collaborates with MindChild on signal analysis.



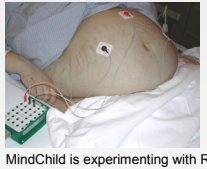
The MindChild monitor on a bedside cart with viewer



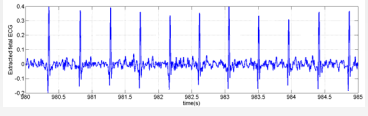
Sensor-selection algorithms identify anatomic locations contributing highest quality fetal ECG signal (red)



A comparison of fetal ECG waveform recorded simultaneously using the scalp electrode and abdominal sensors

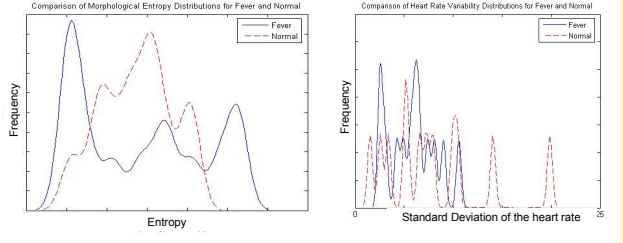


MindChild is experimenting with Red Dot™ adhesive electrodes and non-adhesive electrodes from Orbital Research (right)



Fetal ECG data recorded using the MindChild monitor

Zeeshan Syed and John Guttag at MIT analyzed morphologic entropy and found that, unlike heart rate variability, entropy of fetal ECG could be used to distinguish women with fever from women who remained afebrile during labor. These data were presented at the Society of Maternal-Fetal Medicine in 2008



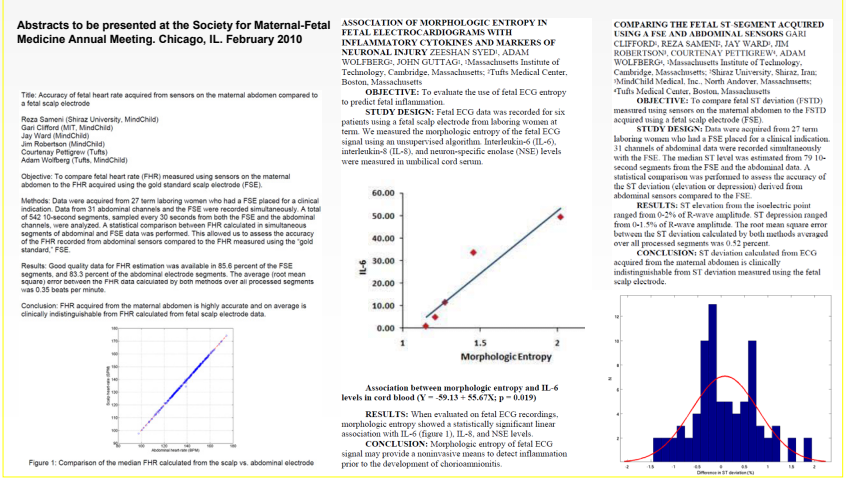
The Journal of Maternal-Fetal and Neonatal Medicine, February 2008; 21(2): 101–104

informa healthcare

A comparison of subjective and mathematical estimations of fetal heart rate variability

ADAM J. WOLFBERG[1,2], DAVID J. DEROSIER[3], TREVOR ROBERTS[4], ZEESHAN SYED[5], GARI D. CLIFFORD[5], DAVID ACKER[4], & ADRE DU PLESSIS[2]

[1]*Tufts-New England Medical Center, Boston, MA, USA,* [2]*Children's Hospital Boston, Boston, MA, USA,* [3]*Brandeis University, Waltham, MA, USA,* [4]*Brigham and Women's Hospital, Boston, MA, USA, and* [5]*Massachusetts Institute of Technology, Cambridge, MA, USA*



Abstracts to be presented at the Society for Maternal-Fetal Medicine Annual Meeting. Chicago, IL. February 2010

Title: Accuracy of fetal heart rate acquired from sensors on the maternal abdomen compared to a fetal scalp electrode

Reza Sameni (Shiraz University, MindChild)
Gari Clifford (MIT, MindChild)
Jay Ward (MindChild)
Jim Robertson (MindChild)
Courtenay Pettigrew (Tufts)
Adam Wolfberg (Tufts, MindChild)

Objective: To compare fetal heart rate (FHR) measured using sensors on the maternal abdomen to the FHR acquired using the gold standard scalp electrode (FSE).

Methods: Data were acquired from 27 term laboring women who had a FSE placed for a clinical indication. Data from 31 abdominal channels and the FSE were recorded simultaneously. A total of 542 10-second segments, sampled every 30 seconds from both the FSE and the abdominal channels, were analyzed. A statistical comparison between FHR calculated in simultaneous segments of abdominal and FSE data was performed. This allowed us to assess the accuracy of the FHR recorded from abdominal sensors compared to the FHR measured using the "gold standard," FSE.

Results: Good quality data for FHR estimation was available in 85.6 percent of the FSE segments, and 83.3 percent of the abdominal electrode segments. The average (root mean square) error between the FHR data calculated by both methods over all processed segments was 0.35 beats per minute.

Conclusion: FHR acquired from the maternal abdomen is highly accurate and on average is clinically indistinguishable from FHR calculated from fetal scalp electrode data.

Figure 1: Comparison of the median FHR calculated from the scalp vs. abdominal electrode

ASSOCIATION OF MORPHOLOGIC ENTROPY IN FETAL ELECTROCARDIOGRAMS WITH INFLAMMATORY CYTOKINES AND MARKERS OF NEURONAL INJURY

ZEESHAN SYED[1], ADAM WOLFBERG[2], JOHN GUTTAG[1], [1]Massachusetts Institute of Technology, Cambridge, Massachusetts; [2]Tufts Medical Center, Boston, Massachusetts

OBJECTIVE: To evaluate the use of fetal ECG entropy to predict fetal inflammation.

STUDY DESIGN: Fetal ECG data was recorded for six patients using a fetal scalp electrode from laboring women at term. We measured the morphologic entropy of the fetal ECG signal using an unsupervised algorithm. Interleukin-6 (IL-6), interleukin-8 (IL-8), and neuron-specific enolase (NSE) levels were measured in umbilical cord serum.

Association between morphologic entropy and IL-6 levels in cord blood (Y = -59.13 + 55.67X; p = 0.019)

RESULTS: When evaluated on fetal ECG recordings, morphologic entropy showed a statistically significant linear association with IL-6 (figure 1), IL-8, and NSE levels.

CONCLUSION: Morphologic entropy of fetal ECG signal may provide a noninvasive means to detect inflammation prior to the development of chorioamnionitis.

COMPARING THE FETAL ST SEGMENT ACQUIRED USING A FSE AND ABDOMINAL SENSORS

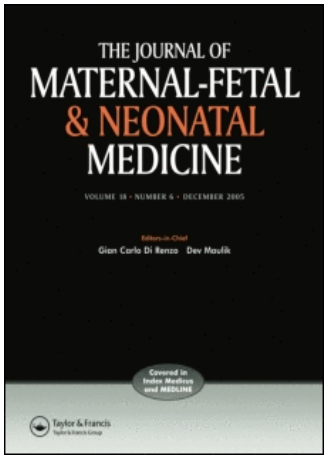
GARI CLIFFORD[1], REZA SAMENI[2], JAY WARD[3], JIM ROBERTSON[3], COURTENAY PETTIGREW[4], ADAM WOLFBERG[4], [1]Massachusetts Institute of Technology, Cambridge, Massachusetts; [2]Shiraz University, Shiraz, Iran; [3]MindChild Medical, Inc., North Andover, Massachusetts; [4]Tufts Medical Center, Boston, Massachusetts

OBJECTIVE: To compare fetal ST deviation (FSTD) measured using sensors on the maternal abdomen to the FSTD acquired using a fetal scalp electrode (FSE).

STUDY DESIGN: Data were acquired from 27 term laboring women who had a FSE placed for a clinical indication. 31 channels of abdominal data were recorded simultaneously with the FSE. The median ST level was estimated from 79 10-second segments from the FSE and the abdominal data. A statistical comparison was performed to assess the accuracy of the ST deviation (elevation or depression) derived from abdominal sensors compared to the FSE.

RESULTS: ST elevation from the isoelectric point ranged from 0-2% of R-wave amplitude. ST depression ranged from 0-1.5% of R-wave amplitude. The root mean square error between the ST deviation calculated by both methods averaged over all processed segments was 0.52 percent.

CONCLUSION: ST deviation calculated from ECG acquired from the maternal abdomen is clinically indistinguishable from ST deviation measured using the fetal scalp electrode.



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Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713453317

A comparison of subjective and mathematical estimations of fetal heart rate variability

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A comparison of subjective and mathematical estimations of fetal heart rate variability

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Abstract

Objectives. To develop a computerized algorithm to quantify fetal heart rate (FHR) variability and compare it to perinatologists' interpretation of FHR variability.

Methods. FHR variability was calculated using data from 30 women who had a fetal scalp electrode placed for a clinical indication, and compared to the assessment of FHR variability from four perinatologists who interpreted paper tracings of the same data. Inter-rater reliability was calculated and receiver–operator curve analysis was done.

Results. Correlation between the computer algorithm's assessment of variability and the perinatologists' assessment (0.27–0.68) was similar to the inter-rater reliability between perinatologists (0.33–0.72).

Conclusions. A computer-based algorithm can assess FHR variability as well as expert clinicians.

Keywords: *Fetal monitoring, variability, fetal heart rate*

Introduction

The normal regulation of the fetal heart rate (FHR) is closely controlled by the central nervous system. Heart rate and rhythm are governed by the sinoatrial node and modulated by autonomic influence. At rest, vagal tone is the dominant source of variation in heart rate, however this variation is affected by the interaction between vagal and sympathetic activity, as well as central respiratory and motor centers, and peripheral oscillations in blood pressure and respirations [1–5].

When continuous FHR monitoring was introduced in the 1970s, there was enormous optimism that the widespread use of this technology would dramatically reduce intrapartum fetal injury and death. Unfortunately, FHR monitoring has not lived up to its initial promise: one meta-analysis of nine randomized, controlled trials comparing FHR monitoring to intermittent auscultation of the fetal heart rate showed that FHR monitoring increases use of cesarean, forceps, and vacuum delivery, but does not reduce perinatal morbidity or mortality [6]. Another similar meta-analysis did find that the use of continuous FHR monitoring decreased the incidence of neonatal seizures, but did not influence the rate of perinatal mortality [7]. This study also showed an association between continuous FHR monitoring and an increased rate of operative delivery. In the intervening 30 years, there have been no clinically significant advances in intrapartum fetal monitoring.

Considerable disagreement persists about what constitutes a non-reassuring fetal heart tracing. This inconsistency is both a reflection of our incomplete understanding of this signal, as well as an impediment to evaluation of FHR as a clinical tool across different studies. However, there is loose consensus that in the presence of FHR accelerations and/or the presence of moderate or marked variability, fetal acidosis is unlikely [8,9].

In spite of a standard definition for components of the FHR tracing [10], another problem with this technique is the poor inter-observer reliability among

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clinicians interpreting FHR tracings [11,12]. Consequently, interpretation of whether an FHR tracing is reassuring, non-reassuring, or ominous remains inconsistent [10].

A number of investigators have described algorithms to quantify components of the FHR tracing [13], and have quantified FHR variability, usually in terms of the mean difference in FHR during a period of time [14–16]. Although a number of these algorithms were able to quantify FHR variability, none have provided a system for directly comparing visually-measured FHR variability using the National Institute of Child Health and Human Development (NICHD) criteria with variability measured using signal processing mechanisms.

There has been recent interest in an automated mechanism for the interpretation of FHR tracing components [17,18], but it is unknown what criteria these systems use to define the components that they are interpreting. This is a difficult proposition because the definitions of the FHR tracing components were described using a system that depends on subjective interpretation by the clinician [10].

Our objective with this study was to correlate the NICHD definition of variability, which is 'quantified' visually as the difference between peak FHR and trough FHR in beats per minute, with a mathematical definition that can be used to standardize the reporting of variability in clinical applications.

Methods

This study was conducted at the Department of Neurology, Children's Hospital Boston, and the Department of Obstetrics and Gynecology, Brigham and Women's Hospital, both in Boston, MA, USA.

Fetal electrocardiogram data were collected during labor using a General Electric Corometrics® 120 fetal monitor, from 30 women who had a scalp electrode placed for a clinical indication, and after analog-to-digital conversion, were recorded digitally at 2000 Hz. Autocorrelation was used to identify the precise peak of the R-wave for each heart beat, and the R–R interval was then calculated, and instantaneous FHR determined calculated for each fetal heart beat.

Mean FHR was calculated over a single 10-min time-period for each subject, and the variance of the heart rate was calculated for the same period. The standard deviation, which is the square root of the variance, was used as the computed measure of FHR variability.

Four perinatologists with recognized expertise and extensive experience in fetal monitoring were provided with printouts of the FHR tracings from the 10-min datasets. The tracings were printed from archived clinical data using the WatchChild™ software system. These clinicians were blinded to the subjects' identifying information, and were unaware of the subjects' clinical outcomes. They had not seen the remainder of the subjects' FHR recordings, and were not shown the corresponding tocometry tracings. Unbeknownst to the expert reviewers, each reviewed 8–12 FHR tracings twice, at least one week apart.

The clinicians were asked to quantify variability for each 10-min tracing (see example, Figure 1). They were also asked to characterize FHR variability during each period using NICHD criteria (absent, minimal, moderate, marked, or sinusoidal). They were provided with a copy of the NICHD criteria to guide their ratings [10].

Intra-rater reliability was calculated using Pearson's r correlation analysis, and a weighted kappa

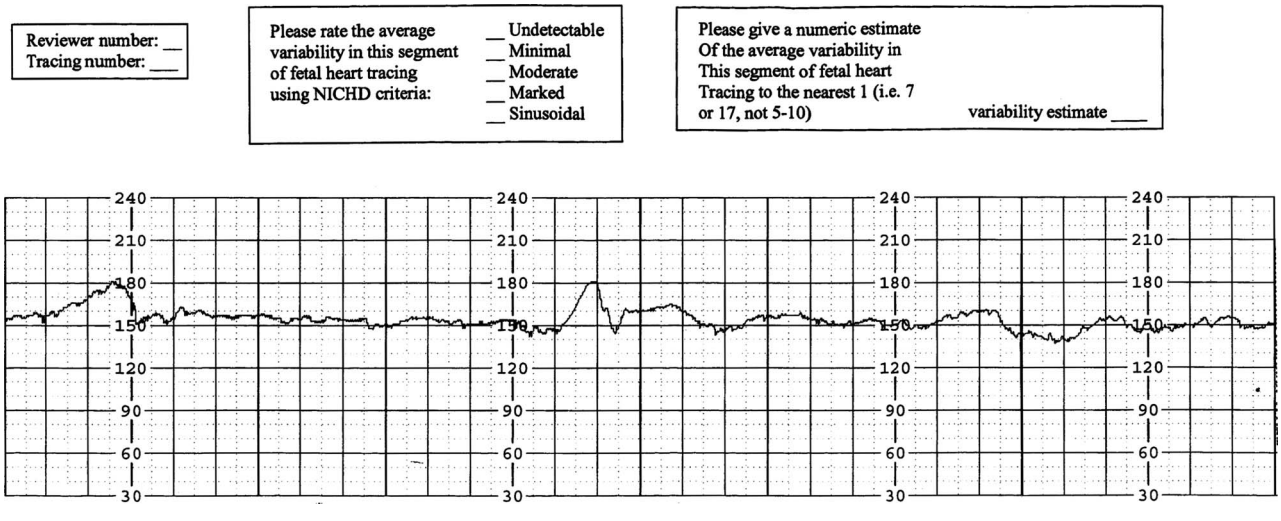

Figure 1. Sample fetal heart rate tracing scored by expert perinatologists.

coefficient was calculated to evaluate intra-rater correlation for the NICHD categorical data, as well as for inter-rater correlation of the categorical data. Intra-class correlation analysis was used to calculate inter-rater correlation for quantitative data, and to correlate the algorithm with the perinatologists' interpretations of the data. Receiver–operator curve analysis was used to compare the algorithm with the perinatologists' categorical interpretations.

This study was approved by the human research committee at our institution.

Results

All subjects were between 35 and 41 weeks estimated gestational age, with a singleton pregnancy. All had a fetal scalp electrode placed for a clinical indication. The Apgar scores at 1 and 5 minutes were greater than 6 for all newborns, and there were no neonatal complications for any of the newborns.

FHR variability ranged from 1.9 beats per minute (bpm) to 19.9 bpm in each 10-min epoch. The perinatologists' assessment of average FHR variability ranged from 1 to 30 bpm. In a few instances, individual perinatologists rated individual tracings as having absent, marked, or sinusoidal variability. However, a majority of the perinatologists' assessments rated each tracing as having either minimal or moderate variability.

The intra-observer reliability when the same reviewer scored the same FHR tracing on separate occasions varied widely, with correlation coefficients ranging from 0.08 to 0.98. Grouping the reviewers together, the intra-observer reliability was 0.77. Similarly, the consistency with which reviewers assigned the same NICHD category of variability to the same tracing ranged from a weighted kappa score of 0.18 to 1.0.

The agreement between reviewers interpreting the same FHR tracing was poor, with a correlation coefficient of 0.44 (range 0.33–0.72). The perinatologist reviewers were also in moderate agreement when assigning NICHD criteria to the tracings, with an overall weighted kappa score of 0.54 (range 0.30–0.58).

There was moderate agreement between the computer algorithm assessment of FHR variability and that of the perinatologists, with a correlation coefficient of 0.62 (range 0.27–0.68) (Table I).

Receiver–operator characteristic analysis demonstrated that a cutoff of 5.0 bpm correctly distinguished minimal from moderate variability approximately 80% of the time when compared to the average assessment of the perinatologists – the gold standard (Figure 2).

Discussion

Poor reliability is perhaps the most glaring weakness in the current system of FHR monitoring. This report is only the most recent in a series of studies over the past three decades demonstrating that even using the same criteria to interpret the same FHR tracing, expert clinicians don't agree with each other, and often don't agree with themselves. For this reason, an algorithm that standardizes the measurement of variability is a useful development – for research on FHR monitoring, and for clinical management of patients during the antepartum and intrapartum periods.

Previous papers have described systems to quantify FHR variability, however most do so in isolation, without direct comparison to human interpretation of the same data [13,15,16,19,20]. Our data demonstrate that it is possible to develop an algorithm for the assessment of variability that is as reliable as the current gold standard of subjective variability assessment – flawed as that system is.

Because nearly 40 years of research has demonstrated that FHR variability is neither sensitive nor specific for hypoxic-ischemic fetal injury, it seems unlikely that a system for quantifying FHR variability would alone make this single test of fetal wellbeing more predictive of an adverse event in labor. However, a more accurate method of describing FHR variability may be useful to clinicians who seek to increase the reliability of their assessment of variability, and to investigators working on advanced monitoring techniques such as ST analysis [21], investigations into power spectrum of FHR [22], and other measures of autonomic status exhibited in the fetal cardiac signal [23].

We are optimistic that ongoing research initiatives will reveal features of the fetal cardiac signal that

Table I. Correlation of numeric variability assessment by expert reviewers and a computer algorithm's assessment of variance (*p*-values).

	Expert average	Expert 1	Expert 2	Expert 3	Expert 4
Computer	0.62 (<0.01)	0.27 (0.19)	0.54 (<0.01)	0.45 (0.03)	0.68 (<0.01)
Expert Avg		0.50 (<0.01)	0.90 (<0.01)	0.86 (<0.01)	0.84 (<0.01)
Expert 1			0.33 (0.07)	0.40 (0.03)	0.37 (0.04)
Expert 2				0.72 (<0.01)	0.72 (<0.01)
Expert 3					0.55 (<0.01)

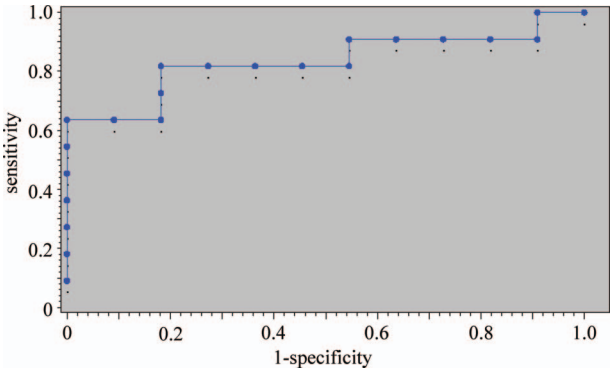

Figure 2. Receiver–operator characteristic analysis of fetal heart rate variability to distinguish minimal from moderate variability.

identify the presence of insult and imminent injury at the level of the myocardium, the brainstem, or the cerebrum. Such endeavors will be quantitative, and we are hopeful that this simple system for quantifying FHR variability will facilitate these important initiatives designed to wring more clinical value from the fetal cardiac signal – the only continuously accessible fetal physiologic signal during labor.

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