Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

A Unified Contraction Characterization for the Identification of Spontaneous Onset of Labor in Term Nulliparous Women via Multi-Channel Electrohysterography and Tocodynamometer

Jinshan XU
Zhejiang University of Technology
Junhua Shen
Zhejiang University
Yiwei Lin
Zhejiang University
Xiaoxia Bai
Zhejiang University
Alain Pumir
ENS de Lyon and CNRS
Baohua Li
lbh19787@zju.edu.cn

Zhejiang University

Article

Keywords: Uterine Contraction, Electrohysterography, Tocodynamometer, Synchrony, Onset of Labor

Posted Date: September 2nd, 2024

DOI: https://doi.org/10.21203/rs.3.rs-4810605/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

A Unified Contraction Characterization for the Identification of Spontaneous Onset of Labor in Term Nulliparous Women via Multi-Channel Electrohysterography and Tocodynamometer

Jinshan XU[1*]; Junhua Shen[2*]; Yiwei Lin[2]; Xiaoxia Bai[2]; Alain Pumir[3†]; Baohua Li[2†]

[1] College of Computer Science and Technology, Zhejiang University of Technology, Hangzhou, 310023, Zhejiang, China.

[2] Department of Obstetrics, Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, 310002, Zhejiang, China.

[3] Laboratoire de Physique, ENS de Lyon and CNRS, 69007, Lyon, France

Author for Correspondence

†Alain Pumir, Address: Laboratoire de Physique, ENS de Lyon and CNRS, 69007, Lyon, France. Email: alain.pumir@ens-lyon.fr

†Baohua Li (Lead contact), Address: Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, 310002, China. Email: lbh19787@zju.edu.cn

*Contributed equally

Conflicts of Interest

We declare no completing interests.

Sources of financial support for the research

This work is supported partially by the opening project of Zhejiang Engineering Research Center of Cognitive Healthcare, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University (No.~2022JJKT01), Natural Science Foundation of China under Grant 62373327 and Zhejiang Provincial Natural Science Foundation under Grant LY24H040003 and LTGY23H040009.

Abstract

Background: Strong and synchronized contractions that occur in the last stage of pregnancy are essential for onset of labor. In clinics, the lack of effective description of these characteristics results in inaccurate prediction of the onset of labor. The commonly used contraction monitoring device tocodynamometer (TOCO) detects contractions with relatively high specificity but is unable to quantify the strength and synchrony. The electrohysterography (EHG) quantifies the myoelectric activities that trigger contractions of muscle cells under the electrodes. Therefore, multiple channel EHG signals are well suited for characterizing the strength and synchrony of uterine contractions via their spatiotemporal pattern.

Object: The purpose of this study was to provide quantitative descriptions of the contraction characteristics and to investigate their significance for predicting the spontaneous onset of labor in nulliparous women.

Study Design: 100 pregnant women with a gestational age of more than 37 weeks were recruited for the study. Multichannel EHG and tocodynamometer recordings were performed simultaneously for 46 of them, both during pregnancy and during labor (defined a time to onset of labor (TTL) less than 24 h). Contractions were identified from the TOCO recordings, and then the frequency and duration of contractions were determined. The multichannel EHG segments under the identified contractile time windows were used to calculate the strength and level of synchrony. Statistical analyses were carried to demonstrate the difference of these variables between the pregnant and labor groups. Multivariate logistic regression was created to provide obstetricians with an assessment tool in predicting spontaneous onset of term labor.

Results: The frequency, duration, strength, and level of synchrony of uterine contractions for 46 pregnant women during their 37 weeks of gestation to the onset of labor were quantified. All constructed features in labor, with the exception of concordance correlation-based synchrony ψ, showed statistically significant differences from those in pregnant phase, with degree of synchrony described by the sample entropy SamEn being the strongest feature for distinguishing pregnant and labor (0.5154 ±0.1720 vs. 0.3555 ±0.1422, $p = 0.00001$). The multivariate logistic regression model constructed from these features showed high significance in identifying the onset of spontaneous labor in nulliparous women, with an AUC value of 0.80.

Conclusion: The contraction properties in terms of frequency, duration, strength, and level of synchrony have been quantitated. Continuous observations on 46 pregnant women throughout their pregnancy demonstrated statistically significant difference between contractions in pregnant and labor phase, which enabled a prediction model on spontaneous onset of labor in term nulliparous women.

Key words: Uterine Contraction, Electrohysterography, Tocodynamometer, Synchrony, Onset of Labor

1. Introduction

The uterus is a unique organ. It provides a relatively stable and calm environment for the development and growth of fetus, when approaching to the final stage, it produces strong contractions throughout the uterus to dilate the cervix and expel the fetus. However, not all uterine contractions could lead a successful delivery. A range of maternal complications, such as dystocia and postpartum hemorrhage are primary due to the lack of efficient uterine contractions in late stage of pregnancy[1]. Consequently, effectively identifying contraction and determining the associated features are of essential importance to the management of pregnancy and labor[2]. Frequency, intensity, duration, and the level of synchrony are considered as good indicators of contractions that enable the proper functioning of the uterus in the different phases of pregnancy[3, 4].

Currently, there are three different technical solutions to the clinical needs of contraction identification and monitory, i.e., Intrauterine pressure catheter (IUPC), tocodynamometer(TOCO) and electrohysterography (EHG)[5]. Among them, the TOCO is the most commonly and routinely used in clinical practice due to its non-invasiveness. In TOCO, a pressure sensor is used to detect the build-up of tensions of the uterine wall caused by contraction. For this purpose, the pressure sensor must be tightly attached to the abdomen wall with an elastic belt. This tightness is uncomfortable for pregnant women. On the other hand, a loose belt significantly impairs measurement accuracy, especially in obese women[6]. IUPC is considered the gold standard in uterine contraction monitoring, as it provides an accurate measurement of contraction frequency, duration, and intensity. However, its clinical application is severely limited by the invasiveness of membrane rupture, which increases the risk of intrauterine infection and placental disruption[7]. Although IUPC shows clear superiority over TOCO in detecting contractions and in measuring contractile strength, a recent published randomized controlled clinical trial (RCT) shows that the IUPC has little effect in reducing the rate of operative deliveries and the use of oxytocin or adverse neonatal outcomes, and in shortening labor duration[8]. The fundamental basis for both TOCO and IUPC in detecting uterine contractions is based on the build-up of intrauterine pressure. This macro parameter (pressure) is not very informative for quantitating the synchrony of uterine contractions. This could explain why the IUPC also has little effect in predicting preterm birth or the onset of labor.

The close relationship between uterine contraction and the fundamental electrical activity at cellular level provides the third way to detect uterine contraction [9]. The electro-hysterography (EHG), a collective manifestation of the electrical activity of uterine myometrium under electrodes placed on the abdomen

of pregnant woman, marks uterine contraction as burst of action potentials. This phenomenon inspired an alternative way of contraction detection. Researchers have attempted to estimate the intrauterine pressure and detect uterine contractions using EHG recordings. These works demonstrate that the EHG has higher sensitivity in detecting true contraction than the TOCO [5, 10]. However, the recorded EHG signals are sensitive to interference from other organs, resulting in high false positive rate[11, 12]. Recently, we proposed an automatic detection method which shows improved precision in true contraction detection while still having a very little power in reducing false positive rate[13].

Although EHG signals are measures of a very localized muscle electrical activities, the spatial information is lost when EHG is used to estimate intrauterine pressure, resulting in a very limited contribution to the clinical requirements of effective contraction management. Attempts to characterize the properties of uterine contractions rather than to identify the occurrence of contraction have shown very promising prospects. For example, Euliano et al. proposed a qualitative description on the direction of uterine contraction using the spatiotemporal information embedded in multichannel EHG signals[14]. Lucovnik et al. went a step further and measured the propagation velocity of contraction, which proved to be very powerful in discriminating preterm labors[15]. However, determining the speed or direction of propagation is a challenge, even in qualitative terms. Despite considerable scientific efforts in the development of algorithms for estimating the speed of propagation[16, 17], no satisfactory solution for practical clinical applications has been found so far.

In vitro observations of the propagation pattern of uterine contractions have led to technical innovations in the characterization of contractions [18]. Eswaran et al developed a magnetomyographic recording system to visualize the spatial distribution of myometrial synchrony[19]. Recently, an electromyometrial imaging system was developed to image the three-dimensional (3D) pattern of uterine contraction[20]. These technologies enable a clear observation of synchronized contractions during labor and suggest the importance of quantitating synchrony of uterine contraction in clinical application. Multiple-channel EHG signals are suitable for this purpose. Recently, we combined the advantages of TOCO in contraction detecting and Multiple-channel EHG in quantitating the synchrony of contractions. By using the simultaneously recorded EHG segments from different locations under the contractile time windows, quantitative description of spatial regularity or synchrony of contractions was obtained and showed a strong ability in predicting imminent labor [21]. In addition to synchrony, the frequency, intensity, and duration of contractions also play important roles in maintaining uterine functionality[1], as demonstrated by Marinescu et al's work who used the expressions of spikes, short-burst, and burst of

electrical activities to assess contraction strength and to relate the strength to cervical length[22].

Despite these pioneer works aiming to correlate characteristics of uterine contraction to clinical needs, there is still a lack of effective methods to non-invasively and precisely quantify contractile intensity, especially in accordance with other characteristics. Based on our recent work on the characterization of synchronous contractions[21], we present here a novel algorithm that provides a unified quantitative evaluations on the contraction frequency, duration, intensity and synchrony. We compare these properties in two patient groups with spontaneous term labor within (recording time-to-labor, TTL<24h) and beyond (TTL≥24h). We then test the feasibility of using the contraction properties to predict the individual probability of a spontaneous onset of labor in term nulliparous women.

2. Material and Methods

General Information

This study was approved by the Ethics Committee of Women's Hospital School of Medicine Zhejiang University in February 2023(Hangzhou, China; IRB-20230052-R). All the methods were performed in accordance with the relevant guidelines and regulations and all subjects signed a written informed consent to participate in the study.

We conducted a prospective continued observational study of subjects with singleton pregnancies, without anomalies and a gestational age of ≥37 weeks. The patients underwent routine prenatal examinations between April 2023 to August 2023 and eventually gave birth in our hospital. A total of 100 patients were initially included in the study based on the following criteria, age (years, ≥18 and <35), body mass index (BMI kg/m^2, ≥18 and <25), gestational age (week, ≥37 and <40), estimated fetal weight <4kg, without uterine scar and without pregnant complication. These patients were asked to perform combined measurements of TOCO and multichannel EHG signals at least twice during the 37 weeks of gestation until the labor stages according to the protocols described later. Among the measurements at least one TOCO and EHG signal must be recorded at a time less than 24 hours before the onset of labor. Patients with TOCO and EHG signals recorded only at a time to labor (TTL) larger than 24h or only at a time to labor (TTL) less than 24h were excluded. Other exclusion criteria include suspected congenital or chromosomal abnormalities, a history of spontaneous preterm birth (PTB), a history of prior cervical surgery.

On the basis of these criteria, 46 patients were included in the study, 36 of whom had normal vaginal deliveries. The remaining 10 patients had cesarean section (CS) delivery even through all of them entered

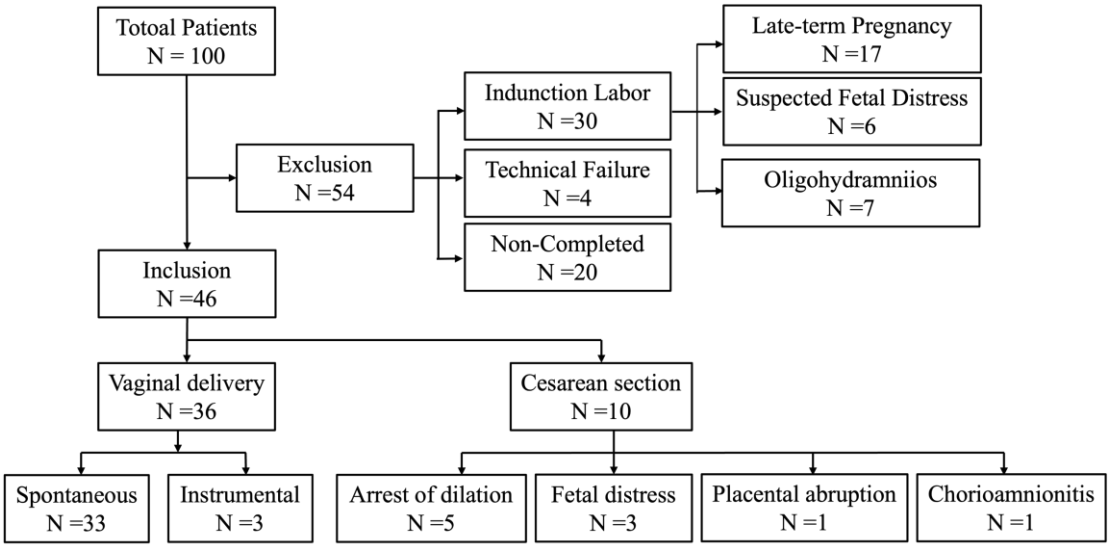


Figure 1 Patient Selection Procedure

in the spontaneous labor stage. Moreover, the decision of CS delivery was given by senior obstetrician (XiaoXia Bai and Baohua Li) for reasons such as arrest cervical dilation (N=5), fetal distress (N=3), placental abruption(N=1) and chorioamnionitis (N=1), according to Obstetric indications. The detailed patient selection procedure is given Figure 1.

Clinical Data Acquisition

As all subjects took regular prenatal examinations at our hospital, their clinical data as well as neonatal characteristics were directly extracted from the hospital's electronic medical record (EMR) system. **Table 1** gives a detailed statistical description of the 46 patients included in the study.

Table 1 Maternal, labor, and neonatal characteristics of the 46 subjects

Category	**n (%)/mean (standard deviation)/median (ranges)**
Maternal characteristics	
Age (years)	29.83 ± 2.74
Gravidity	1 (1, 6)
Parity	0 (0, 2)
Pre-gestational BMI (kg/m^2)	21.30 ± 1.81
Pre-delivery BMI (kg/m^2)	26.60 ± 2.78
Gestational age of delivery (days)	278.89 ± 4.82
Labor characteristics	
TTL (min)	198 (60, 1337)
TTD (min)	820 (293, 2432)

Oxytocin augmentation	23 (50%)
Epidural analgesia	34 (73.91%)
ROM	17 (36.96%)
First stage of labor* (min)	450 (145, 1265)
Second stage of labor* (min)	63 (4, 189)
Delivery mode	
Spontaneous vaginal delivery	33 (71.74%)
Instrumental vaginal delivery	3 (6.52%)
Cesarean section	10 (21.74%)
Neonatal characteristics	
Neonatal gender	
female	26 (56.52%)
male	20 (43.48%)
Neonatal birthweight (g)	3371.74 ± 344.98
1-min Apgar	10 (7, 10)
5-min Apgar	10 (10, 10)

BMI, Body mass index; TTL, the recording time to labor; TTD, the recording time to delivery; ROM, Rupture of membranes.

* Only 36 of whom delivered vaginally were included, and the data further analyzed.

Electrical and Contractile Signal Acquisition

Uterine Electrohysterography was collected by Ag/AgCle electrodes placed on the abdomen of pregnant women. To enable a good representation of the spatial-temporal patterns of uterine contraction[21], 8 electrodes were adopted, with 6 electrodes forming a circle of radius 3cm around the navel, and the other two serving as reference and ground (Figure 2). Recordings were made for at least 30 minutes using the 8-channel Cyton Biosensor Board (OpenBCI), which first digitizes the measured voltages as 16-bit integers and records them with a sampling frequency 200Hz. To ensure a high signal-to-noise ratio, the skin was carefully prepared with 75% alcohol before placing the electrodes. At the same time, uterine contractions were monitored using a commercial Tocodynamometer (EDAN: MT-811).

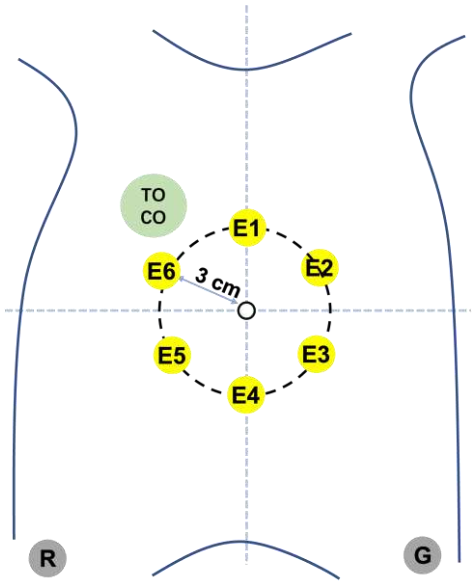


Figure 2. Electrodes and TOCO configuration in practical electrical activity and uterine contraction monitoring

Contraction Property Characterization

Uterine contractions were independently identified from the recorded 30-minute TOCO traces by two senior obstetricians (Junhua Shen and Liangshan Mu) based on the following criteria:1) A significant increase in abdominal pressure indicated by a TOCO signal larger than 30; 2) The TOCO segment has a rough Gaussian shape without sharp edges within a time interval; 3) The duration must be greater than 10 s. Each of the identified contraction j was marked by two-element tuple (t^{js}, t^{je}), where t^{js} and t^{je} refer respectively to the time where the j^{th} contraction starts and terminates. So, all the n contractile time windows identified from one TOCO trace can be represented as $[(t^{1s}, t^{2e}), (t^{2s}, t^{2e}), \ldots, (t^{ns}, t^{ne})]$. This identification enabled a straightforward definition of contraction frequency, the number of contractions within 30 minutes n and average contraction duration Δt defined as:

$$\Delta t = \frac{\sum_{j=1}^{n}(t^{je} - t^{js})}{n} \quad (1)$$

The root mean square (RMS) of the EHG segment $\mathbf{x}^j{}_c = [x_1, x_2, \ldots, x_N]^j$ from channel c under the contractile time window (t^{js}, t^{je}) was used to describe the contraction intensity of uterine myometrium under electrode c during the time interval (t^{js}, t^{je}). Taking an average over all channels and contractile time windows, these localized contractions gave us a quantitative description of macro contraction strength RMS. Following reference [21], the sample entropy based synchrony SamEn and Concordance correlation based synchrony ψ of uterine contractions could also be obtained from these contractile EHG segments from different channels. Detailed definition of contractile EHG segments was

illustrated in Figure 3, where contractile time windows identified from the TOCO signals are marked in light red. Only these segments were used to build quantitative descriptions of contraction. The other parts were discarded, even though there seemed to be bursting activities (the blue regions).

Statistics

Statistical analysis was carried out using IBM SPSS 19.0 for Windows (IBM Corp., Armonk, NY, USA). The data were shown as number (percentage), mean (standard deviation) and median (ranges), as appropriate. Continuous data were tested for normality using the Kolmogorov-Smirnov test. The paired, 2-tailed *t* test or the Wilcoxon matched –pairs test according to continuous data distribution were used to compare the characteristics of uterine contractions between pregnancy and labor groups. Furthermore, a receiver operating characteristic (ROC) curve was constructed to introduce different cut-off values to the patients, and the area under curve (AUC) was calculated to quantitate the ability of these quantities in discriminating onset of labor. Additionally, in the univariate and multivariate analyses, Poisson Regression was used to identify predictors for labor, and relative risk (RR) and 95% confidence intervals (CIs) were calculated. Finally, all statistical tests were two-sided, and P values < 0.05 were considered to be statistically significant (* significant $P< 0.05$; ** significant $P< 10^{-3}$; *** significant $P< 10^{-5}$).

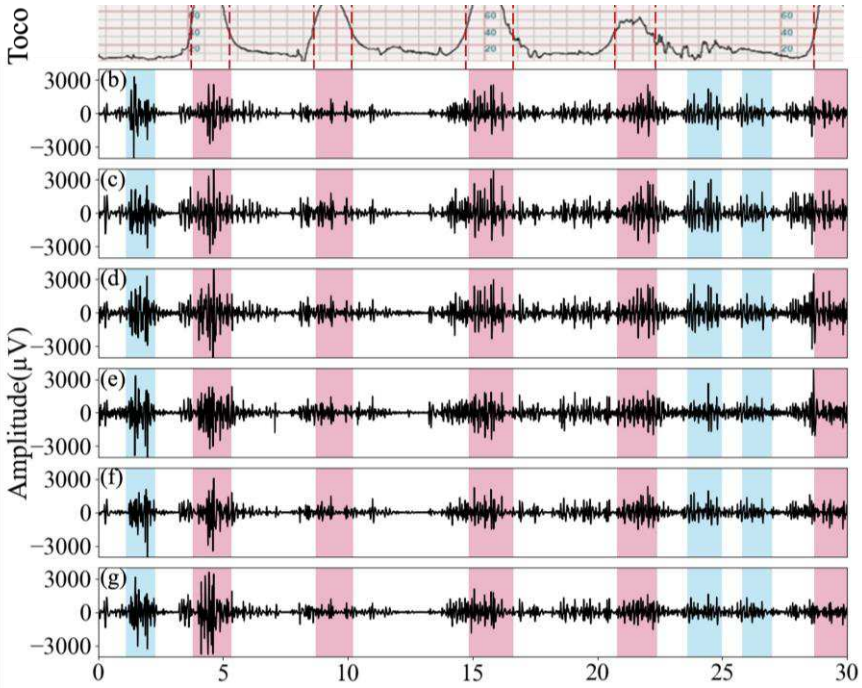


Figure 3. Definitions of contractile EHG segments from TOCO trace. Light red shaded regions mark the contractile time windows identified from TOCO.

3. Results

General Characteristics of Contractions in Pregnancy and Term Labor Patients

A total of 117 combined examinations with simultaneous multichannel EHG and TOCO recordings were performed during the entire pregnancies of the 46 patients. According to the difference of the recording time to onset of labor (TTL), these recordings were divided into two groups, i.e., pregnancy and labor, with the criteria TTL>24h and TTL≤ 24h, respectively. In total, there 71 recordings in the pregnancy group had and 46 recordings in the labor group. In the pregnancy group, the average gestational age at signal recording was 269.5 ± 5.8 days, which was significantly different from that of the signals in the labor group (278.3 ± 4.6 days, p <0.0001).

Since all the signals from both groups came from the same subjects, they had the same demographic and clinical characteristics. However, the characteristics of the uterine contractions that we determined from the multichannel EHG segments under contractile time windows showed differences between the two groups. Figure 4 shows the mean values of the constructed quantitative characteristics with 95% confidence intervals (CIs) in the pregnancy and labor groups and the number of asterisks marking the

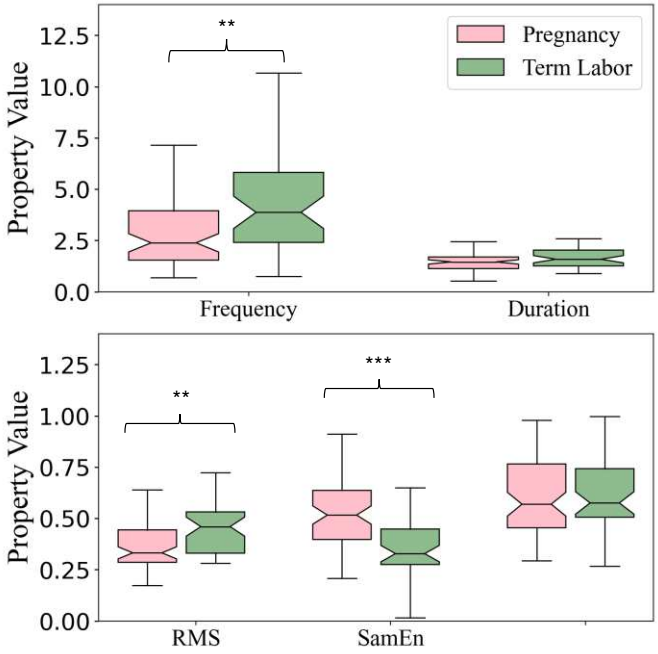


Figure 4 Properties of Contraction in Pregnancy and Term Group.
* *Significant ($p < 0.05$)*
** *Significant ($p < 10^{-3}$)*
*** *Significant ($p < 10^{-5}$)*

level of statistical significance between groups. The contraction strength (characterized by RMS), frequency and sample entropy-based synchrony SamEn demonstrate strong power in predicting imminent labor in 24 hours. Although contraction duration might contribute to a successful prediction of

imminent labor, its predictive power is relatively low. However, the concordance correlation-based synchrony ψ show no difference between the two groups ($p = 0.564$). Table 2 gives a detailed comparison of the properties of uterine contractions between the pregnancy and term labor groups.

Table 2 Contraction Properties in P

regnancy and Labor Groups

Features	Pregnancy(n=71)	Term(n=46)	F-Value	p-Value
Strength	0.3799±0.1247	0.4712±0.1454	13.105	<0.001
Frequency	2.7841 ± 1.7839	4.6425 ± 3.3475	15.086	<0.001
Duration	1.5247± 0.6647	1.9524 ± 1.5913	4.0540	0.04602
SamEn	0.5154 ±0.1720	0.3555 ±0.1422	27.523	<0.00001
ψ	0.5980 ±0.1849	0.6180 ±0.1788	0.3350	0.564

Clinical Values in Term Labor Prediction

The statistical differences of the features of contraction between the pregnancy and labor groups suggest their clinical values in predicting imminent term labor patients. A Receiver Operating Curve (ROC) of each property is plotted in Figure 5 to show its ability in predicting imminent term labor patients. The

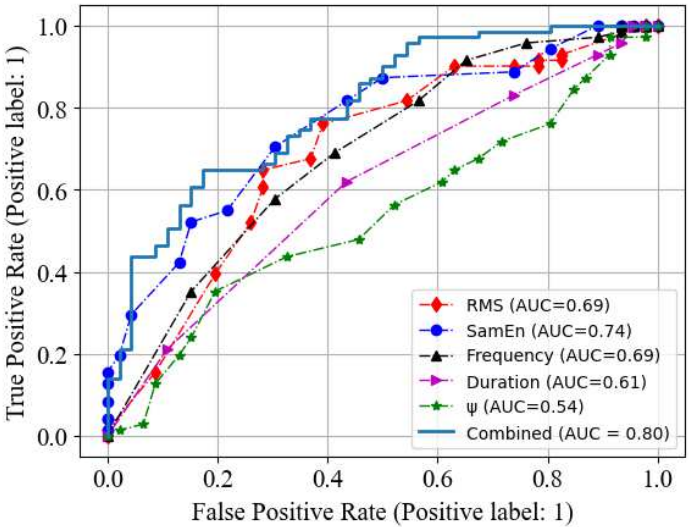


Figure 5 The ROC curves for Contraction Properties to Predict Imminent Term Labor

area under curve (AUC) of contraction strength RMS, synchrony SamEn and ψ, frequency and duration are 0.69, 0.74, 0.54, 0.69 and 0.61, respectively. Their abilities in predicting imminent term labor were further confirmed by both the univariate and multivariate relative risk analysis shown in Table 3. Furthermore, when a multivariate logistic regression model constructed using the most significant variables, i.e., Frequency, SamEn and RMS, a stronger power in term prediction, with an AUC value of

0.8, is obtained.

Table 3 Contraction Properties related to Term Labor Prediction Using Univariate and Multivariate Analysis

Property	p-Value	Univariate RR	p-Value	Multivariate RR[a]	p-Value	Multivariate RR[b]
Frequency	1.720e-4	2.0(1.2~3.1)	1.55e-3	0.678 (0.53~0.86)	1.53e-3	0.679(0.534~0.863)
Duration	4.640e-2	1.6(1.0~2.5)	2.15e-1	0.648 (0.33~1.29)	2.11e-1	0.646(0.326~1.282)
SamEn	7.164e-7	2.8(1.7~4.6)	6.20e-4	346.7 (12.2~9875.6)	6.06e-4	348.8(12.28~9906.9)
RMS	4.394e-4	2.5(1.6~3.9)	6.74e-3	0.008(0.0002~0.266)	5.68e-3	0.008(0.0002~0.246)
ψ	5.634e-1	1.7(0.9~3.1)	9.22e-1	0.878 (0.066~11.73)		

[a] Regression model included all variables presented in the table; [b] Regression model included all variables in presented in the table except ψ, because ψ and SamEn are all used to describe synchrony.

Relationship between gestational age and contraction properties

The successful expulsion of fetus requires forceful and synchronized contractions appear periodically. The linear correlation coefficients between the contraction properties and the gestational age at measurement were calculated and shown in Figure 6. The results reveal the evolutional pattern of uterine contractions toward final delivery. As lower entropy corresponds to more regularity, the negative correlation coefficient of SamEn implies that uterine contractions become more regular and synchronized toward the onset of labor. The positive values of the correlation coefficients of other properties also support more powerful, frequent, and longer-lasting uterine contractions at last stage of pregnancy.

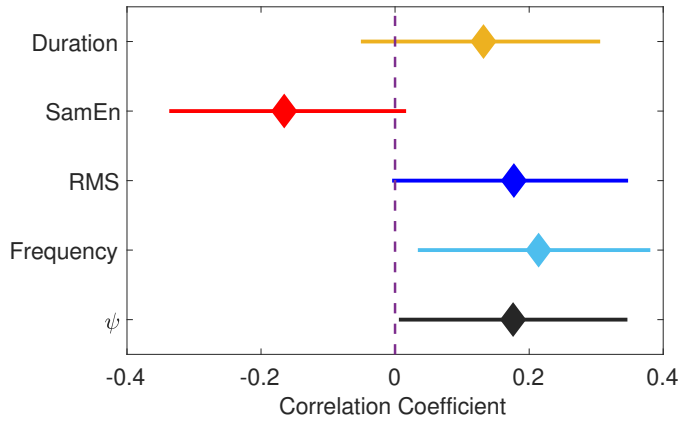


Figure 6 Correlation Coefficient between Contraction Properties and Gestational age

4. Discussion

Principle finding

In this study, we proposed a quantitative description of the properties of uterine contractions by combining the advantages of the multiple channels eletrohysterography and tocodynamometer. We then

analyzed their changes in 46 pregnant women throughout the pregnancy of gestational age ≥37 weeks to labor stage. We found that the frequency, duration, strength, and the level of synchrony of contractions are correlated to gestational age and can characterize the stages of pregnancy. Using one of these properties to predict the imminent term labor within 24h gave an AUC value as high as 0.74. A multivariate logistic regression model that combines the strength (RMS), frequency and synchrony (SamEn) of uterine contractions demonstrated higher predictive power of imminent labor (AUC =0.8).

Results in the context of what is known

Forceful and synchronized uterine contractions have long been known as key factors contributing to the onset of the final delivery of fetus[4, 23]. As the electrical bursting activities of uterine myometrium fully determine the frequency, duration and strength of contractions[9], different methods have been proposed to characterize uterine contractions using the external recordings of these activities, i.e., EHG[24, 25], or to explore the relationship between some quantitative descriptions of the EHG signal and the clinical outcomes[26]. However, there still does not exist any matured EHG based diagnostic applications. One possible reason might be the lack of an effective measurement of characteristics of contractions related to the expulsion of fetus. The spatial-temporal patterns of multi-channel EHG segments under contractile time windows provide a quantitative description of the characteristics, enabling the prediction of imminent term labor. Our preliminary exploration on a publicly available dataset has demonstrated the potential clinical application of the quantitative description of synchrony of contractions[21].

Toward delivery, gap junctions between uterine myometrium cells increase significantly, facilitating the propagation of action potentials. Despite that the mechanism leading to globally synchronized contractions is still not clear[12], toward late pregnancy, more cells participate in contractile activities, leading to an increase in strength and synchrony[27]. The results shown in this paper provide quantitative evidence to evolution patterns of uterine contraction during pregnancy.

Clinical implications

Monitoring uterine contractions is essential to the management of pregnancy. As contractions appear throughout the whole process of pregnancy, discriminating contractions from those leading to imminent term labor is critical to obstetrical practice. Although, obstetricians are aware of the importance synchronized and forceful contractions in deciding the onset of labor, no effective prediction on the onset of labor could be given due to the lack of effective measurement of contraction properties. TOCO is a frequently used tool in contraction monitoring, but it gives the information of contraction frequency and duration with relatively low precision, comparing to the golden standard IUPC[28]. Although EHG signals are more sensitive to contractions, the recorded EHG signals are usually contaminated by

different types of noises which severely deteriorate existing methods in characterizing contraction properties[29, 30].

In this study, we combined the advantages of TOCO and multi-channel EHG to characterize the frequency, duration, strength, and synchrony of contractions, inspired by our previous study carried out on the public available Icelandic EHG database [21]. Our clinical observations on 46 pregnant women with a total of 117 simultaneous recordings of multi-channel EHG and TOCO signals further confirmed their power in predicting imminent term labor.

Research implications

Electrohyterography has long been believed to be an evolutionary direction in obstetrics[12]. It has been receiving research efforts from all different research areas[31]. However, most of the existing works focus on extracting features from EHG signals and creating a mapping between those features and the clinical outcomes. The current study focuses on characterizing properties of uterine contractions, especially on quantitating the frequency, duration, strength, and synchrony of contractions, by unifying the unique advantages of TOCO in reliable detection of uterine contractions and multiple channels electrohysterography in providing spatial-temporal information of contractions. The proposed method provides an effective way of quantitating obstetricians' experience in assessing uterine contractions. The power of these quantities in discriminating imminent labor shown in this study could open new research direction for EHG signal analysis and clinical applications.

Strength and Limitations

The current study proposed a method, which combines the advantages of TOCO in reliable detection of uterine contractions and multiple channels electrohysterography in providing spatial-temporal information of contractions, to characterize the frequency, duration, strength, and level of synchrony of contractions and presented a comprehensive assessment on these properties in term nulliparous women with spontaneous onset of labor. The results demonstrated that contraction frequency, duration, strength, and level of synchrony are essential factors in intriguing term labor. The proposed method not only overcomes the disadvantages of IUPC as invasiveness, but also provides useful insights to clinical practice.

The main limitation is the limited sample size and single central study. We are planning to conduct a prospective multi-central study with a larger size of pregnant women in general population, identifying our findings and improving clinical outcomes. Secondly, the propagation direction of EHG signals has not been included in the present study. Euliano et al. reported the observation of the downward

propagation of EHG signals[14], implying the importance of recruiting it as a contributor to an effective description of uterine contraction. Although we have introduced an effective method in quantitating the synchrony of uterine contraction, our study has little power in revealing the origin of synchronized contraction. The proposed method seems in favor with the electro-mechanical theory[32], as the TOCO provides the mechanical information, while the EHG provides the information of electrical coupling. although there are works rejecting this hypothesis by arguing the fundal dominance and downward progression[33]. No matter what the underlying mechanism is, the successful delivery requires complete synchronization of both electrical and mechanical activities.

Conclusion

The contraction properties in terms of frequency, duration, strength, and level of synchrony have been quantitated via a combined utilization of tocodynamometer and multichannel electrohysterography. Continuous observations on 46 pregnant women throughout their pregnancy revealed a continuous progress toward a more forceful, frequent, and synchronized contractions toward the final stage of pregnancy (onset of labor). In addition, we also demonstrated statistically significant difference of contractions between pregnant and labor phase, in terms of the proposed quantitative descriptions. A model for predicting the spontaneous onset of labor in term nulliparous was established and showed acceptable precision.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data related to the current study are publicly available at https://github.com/DenierXu/EHG_Data_from_ZJU.

References

1. Rosen, H. and Y. Yogev, *Assessment of uterine contractions in labor and delivery.* American Journal of Obstetrics and Gynecology, 2023.
2. Gülümser, C., M. Yassa, and t.W.I.C.A.W. Group, *Clinical management of uterine contraction abnormalities; an evidence-based intrapartum care algorithm.* BJOG: An International Journal of Obstetrics & Gynaecology, 2022. **DOI:10.1111/1471-0528.16775**(n/a).

3. Malik, M., M. Roh, and S.K. England, *Uterine contractions in rodent models and humans.* Acta Physiologica, 2021. **231**(4): p. e13607.
4. Marinescu, P.S., et al., *Contraction Synchronization Predicts the Onset of "True" Labor.* Reproductive Sciences, 2021. **28**(SUPPL 1): p. 221A-221A.
5. Euliano, T.Y., et al., *Monitoring uterine activity during labor: a comparison of 3 methods.* American Journal of Obstetrics and Gynecology, 2013. **208**(1).
6. Aina-Mumuney, A., et al., *The Impact of Maternal Body Mass Index and Gestational Age on the Detection of Uterine Contractions by Tocodynamometry: A Retrospective Study.* Reproductive Sciences, 2016. **23**(5): p. 638-643.
7. Mokhtari, N., et al., *Intraamniotic Infection Rates after Intrauterine Pressure Catheter with and without Amnioinfusion.* American Journal of Perinatology, 2021. **38**(03): p. 212-217.
8. Hautakangas, T., et al., *Intrauterine versus external tocodynamometry in monitoring labour: a randomised controlled clinical trial.* Bjog-an International Journal of Obstetrics and Gynaecology, 2020. **127**(13): p. 1677-1686.
9. Garfield, R.E. and W.L. Maner, *Physiology and electrical activity of uterine contractions.* Seminars in Cell & Developmental Biology, 2007. **18**(3): p. 289-295.
10. Hadar, E., et al., *A comparison between electrical uterine monitor, tocodynamometer and intra uterine pressure catheter for uterine activity in labor.* Journal of Maternal-Fetal & Neonatal Medicine, 2015. **28**(12): p. 1367-1374.
11. Tylcz, J.-B., et al., *An automatic method for the segmentation and classification of imminent labor contraction from electrohysterograms.* IEEE Transactions on Biomedical Engineering, 2019. **67**(4): p. 1133-1141.
12. Young, R.C., P.S. Marinescu, and N.S. Seligman, *Monitoring uterine contractions during labor: current challenges and future directions.* American Journal of Obstetrics and Gynecology, 2023. **228**(5, Supplement): p. S1192-S1208.
13. Chen, Z., et al., *Automatic detection and characterization of uterine*

contraction using Electrohysterography. Biomedical Signal Processing and Control, 2024. **90**: p. 105840.

14. Euliano, T.Y., et al., *Spatiotemporal electrohysterography patterns in normal and arrested labor.* American Journal of Obstetrics and Gynecology, 2009. **200**(1): p. 54. e1-54. e7.
15. Lucovnik, M., et al., *Noninvasive uterine electromyography for prediction of preterm delivery.* American journal of obstetrics and gynecology, 2011. **204**(3): p. 228. e1-228. e10.
16. Rabotti, C., et al., *Modeling and Identification of the Electrohysterographic Volume Conductor by High-Density Electrodes.* Ieee Transactions on Biomedical Engineering, 2010. **57**(3): p. 519-527.
17. Rabotti, C., et al. *Identification of the electrohysterographic volume conductor by high-density electrodes*. in *4th European Conference of the International Federation for Medical and Biological Engineering (ECIFMBE)*. 2008. Antwerp, BELGIUM.
18. Lammers, W.J.E.P., et al., *Patterns of electrical propagation in the intact pregnant guinea pig uterus.* American Journal of Physiology-Regulatory Integrative and Comparative Physiology, 2008. **294**(3): p. R919-R928.
19. Eswaran, H., et al., *Extraction, quantification and characterization of uterine magnetomyographic activity—A proof of concept case study.* European Journal of Obstetrics and Gynecology and Reproductive Biology, 2009. **144**: p. S96-S100.
20. Wang, H., et al., *Noninvasive electromyometrial imaging of human uterine maturation during term labor.* Nature Communications, 2023. **14**(1).
21. Shen, J., et al., *Multi-channel electrohysterography enabled uterine contraction characterization and its effect in delivery assessment.* Computers in Biology and Medicine, 2023. **167**: p. 107697.
22. Marinescu, P.S., et al., *Mid-trimester uterine electromyography in patients with a short cervix.* American Journal of Obstetrics & Gynecology, 2022. **227**(1): p. 83.e1-83.e17.
23. Smith, R., et al., *Why the heart is like an orchestra and the uterus is like a soccer crowd.* American journal of obstetrics and gynecology, 2015. **213**(2): p. 181-185.

24. Euliano, T.Y., et al., *Monitoring uterine activity during labor: clinician interpretation of electrohysterography versus intrauterine pressure catheter and tocodynamometry.* American journal of perinatology, 2016: p. 831-838.
25. Esgalhado, F., et al., *Uterine contractions clustering based on electrohysterography.* Computers in Biology and Medicine, 2020. **123**: p. 103897.
26. Qian, X., et al., *Quantitative analysis for grading uterine electromyography activities during labor.* American Journal of Obstetrics & Gynecology MFM, 2023. **5**(2): p. 100798.
27. Singh, R., et al., *Self-organized transition to coherent activity in disordered media.* Physical Review Letters, 2012. **108**(6): p. 068102.
28. Moni, S.S., et al., *Noninvasive monitoring of uterine electrical activity among patients with obesity: a new external monitoring device.* American journal of obstetrics & gynecology MFM, 2021. **3**(4): p. 100375.
29. Mischi, M., et al., *Dedicated entropy measures for early assessment of pregnancy progression from single-channel electrohysterography.* IEEE Transactions on Biomedical Engineering, 2017. **65**(4): p. 875-884.
30. Rabotti, C., et al., *Modeling and identification of the electrohysterographic volume conductor by high-density electrodes.* IEEE Transactions on Biomedical Engineering, 2009. **57**(3): p. 519-527.
31. Xu, J., et al., *Review on EHG signal analysis and its application in preterm diagnosis.* Biomedical Signal Processing and Control, 2022. **71**: p. 103231.
32. Young, R.C. and P. Barendse, *Linking myometrial physiology to intrauterine pressure; how tissue-level contractions create uterine contractions of labor.* PLoS computational biology, 2014. **10**(10): p. e1003850.
33. Zhang, M., et al., *Estimating uterine source current during contractions using magnetomyography measurements.* PloS one, 2018. **13**(8): p. e0202184.