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Analysis of Electrohysterographic Signal Propagation Direction during Uterine Contraction: the Application of Directed Information

Yuhang Xu[1] Dongmei Hao[2] Dingchang Zheng[1]

***Abstract*— The potential of using the information of uterine contractions (UCs) derived from electrohysterogram (EHG) has been recognized in early detection of preterm delivery. A better understanding of the conduction property of EHG is clinically useful for developing advanced methods to achieve a reliable prediction of preterm delivery. In this paper, a method to analyze the destination of EHG propagation has been proposed via the estimation of directed information (DI) between each pair of neighboring channels with a novel propagation terminal zone (PTZ) identification algorithm. The proposed method was applied to experimental data from the Icelandic 16-electrode EHG database. The results demonstrated that for more than 81.8% participants, the PTZ was identified along the medial axis of uterus, among which more than half have their PTZ determined in the center between the uterine fundus and public symphysis, which indicated a great probability of propagation of EHG signals towards the center of uterus plane.**

***Clinical relevance*— This study makes a fundamental contribution for predicting preterm delivery, which can provide improvement in obstetric care towards pregnancy monitoring.**

I. INTRODUCTION

Inappropriately early activation of the uterus can result in preterm birth which affects an estimated 15 million babies world-wide every year [1], increases the risks of maternal and neonatal mortality as well as morbidity [2]–[6]. In order to reduce the incidence of preterm birth, medical treatment, such as tocolytic agents and corticosteroids which inhibit uterine contractions (UCs), have been used as obstetric interventions to temporarily delay childbirth. Therefore, the early detection of preterm delivery is of great importance, depending on which, the timely treatment could be introduced.

So far, the most effective way to assess UCs for preterm labor diagnosis is by using the intrauterine pressure (IUP) catheters. However, the technique is invasive which involves rupture of the membranes and thus increasing the risk of intrauterine infection, injury to the fetus or accidental induction of labor [7]. Other methods for predicting preterm labor include noninvasive estimation of IUP, cervical length measurements, tocodynamometry, fibronectin tests, measurements of the frequency of UCs and methods based on analyzing the electrical activity of UCs [8]–[13]. Although these measurements are noninvasive, they suffer from several limitations and are not reliable for accurate preterm labor prediction. Therefore, there is a urgent need to develop alternative methods for the prediction of preterm labor.

As a potential diagnostic tool for monitoring labor, electrohysterogram (EHG), which records uterine electrical activity externally on the abdomen, has been considered in several studies regarding its use for discriminating between effective (leading to true labor and delivery) and ineffective (physiological and unproductive) UCs [14]–[22]. Most of the publications focused mainly on signal processing, including the analysis in time and/or frequency domains without a full understanding of the normal EHG physiology during contractions. The propagation properties of EHG signals have demonstrated their potential in distinguishing the productive UCs from the unproductive UCs [23]–[26]. However, no agreed propagation direction has been found [15], [27]–[29].

In this study, we propose to estimate the directed information (DI), which has been used to analyze causal interactions between EEG channels recently, between each pair of EHG signals from neighboring electrodes and determine the most ”terminal” position by using an identification algorithm that calculates the flow of information with regard to each electrode and compares the significance of their surround-inward flow. In this manner, we investigate the propagation direction of EHG signals by discovering the terminal of the flow of information within the recording area, which is particularly effective in the case that the electrodes cannot cover the whole uterus, but are placed on a small region of the abdomen for minimizing the discomfort induced to the pregnant women. The method is applied to experimental data collected from pregnant women to determine the location towards which the EHG signals propagate during normal contractions.

II. METHODOLOGY

A. Dataset and EHG segmentation

The data used for the study were from the Icelandic 16-electrode EHG database [30]. EHG was recorded from 45 pregnant women using a 4×4 monopolar electrode matrix placed on the surface of abdomen. Fig. 1 shows the position of the sixteen electrodes. The third column of electrode matrix (electrodes 9 to 12) was desired to be placed on the medial axis of uterus with the $10th-11th$ pair of electrodes half way between the uterine fundus and public symphysis. EHG signals were passed to a digital converter and sampled at 200 Hz. External tocodynamometry (TOCO) was recorded simultaneously using a tocodynamometer attached to the abdomen. Two to seven recordings were obtained for

[1]Yuhang Xu and Dingchang Zheng are with Center for Intelligent Healthcare, Coventry University, Coventry, UK yuhang.xu@coventry.ac.uk, dingchang.zheng@coventry.ac.uk.

[2]Dongmei Hao is with College of Life Science and Bioengineering, Beijing University of Technology, Beijing, China haodongmei@bjut.edu.cn

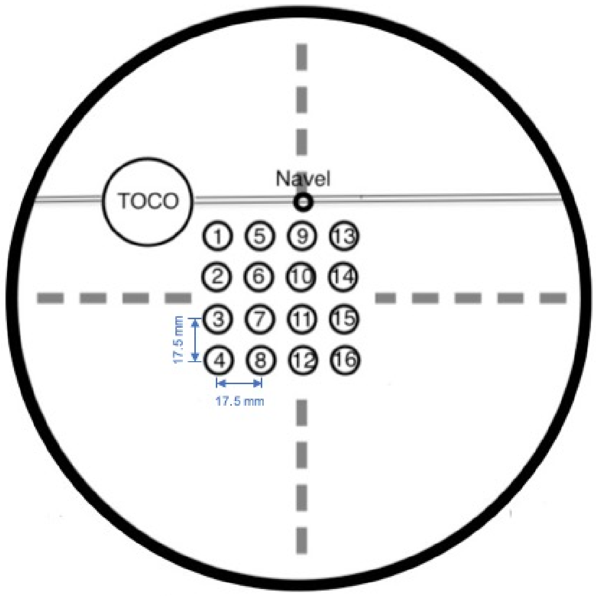

Fig. 1. Illustration of the desired position of 4×4 electrode matrix and tocodynamometer [30].

each participant at different gestational weeks during the third trimester of pregnancy and during labor. A detailed description of the experiments for data collection can be found in [30].

According to the TOCO signal and UC annotation, two clinicians were asked to identify the UC-associated TOCO peaks [31] and only those with their full agreement were counted and processed further. Next, EHG recordings from a pregnant woman of which the number of agreed UC-associated TOCO peaks was more than or equal to 20 were considered for further analysis. EHG segments were then obtained by a 20 s window that begins 10 s before and ends 10 s after the TOCO peaks.

B. DI estimation

The directed information from a random sequence X^n to another random sequence Y^n is defined as

$$I(X^n \to Y^n) \triangleq \sum_{i=1}^{n} I(X^i; Y_i \mid Y^{i-1}) \quad (1)$$

$$= H(Y^n) - H(Y^n \parallel X^n), \quad (2)$$

where $H(Y^n) = \sum_{i=1}^{n} H(Y_i|Y^{i-1})$ is the entropy of Y^n and $H(Y^n \parallel X^n) = \sum_{i=1}^{n} H(Y_i|Y^{i-1}, X^i)$ is the causally conditional entropy [32]. Throughout, we use capital letters for random variables and lowercase letters for their realizations. We denote the sequence of the first i sources from data $X_1, X_2, \cdots$ as $X^i = [X_1, X_2, \cdots X_i]$. According to the interpretation of conditional entropy, the directed information from X^n to Y^n defined as (1) measures the improvement in the prediction of Y_i given the past samples Y^{i-1}, when samples X^i are also available.

In this study, we used one of the estimators of the directed information rate $\overline{I}(X^n \to Y^n) = \frac{1}{n} I(X^n \to Y^n)$ introduced in [33], which is defined as:

$$\hat{I}(X^n \to Y^n) \triangleq \frac{1}{n} \sum_{i=1}^{n} D(Q(y_i \mid x^i, y^{i-1}) \parallel Q(y_i \mid y^{i-1})), \quad (3)$$

where $D(p \parallel q) = E_p[\log \frac{p(x)}{q(x)}]$ is the relative entropy between distribution $p(x)$ and $q(x)$, and $Q(y_i \mid y^{i-1})$ denotes the estimate of the conditional probability mass function (pmf) of y_i given the observation y^{i-1}. This is estimated by the Context-Tree Weighting algorithm [33], [34]. The depth of the context tree D indicates the memory of the model, i.e., the number of past samples included in the sequences x^i and y^{i-1} in (3). The estimator $\hat{I}$ in (3) is always nonnegative.

The DI rate $\overline{I}(X^{n-1} \to Y^n)$ between each pair of neighboring EHG channels was estimated using the DI estimator $\hat{I}$ in (3) from 20 s-long windows. To this end, we first computed the discrete derivative of the EHG signals by looking at first-order difference between successive samples. Then, the derivative was quantized into three levels, namely -1, 0 and 1 using equal frequency binning method [35]. In order to minimize the computational complexity and reduce the variance of the directed information rate, the derivative sequences were down-sampled by a factor of 30 and the results were obtained by averaging over the 30 subsequences. The factor of 30 was selected also to keep the main frequency components of EHG activities ($0.1 - 3$ Hz) remained [15]. Since the longest distance between a pair of neighboring EHG electrodes is 2.47 cm along the diagonal and the EHG conduction velocity during contractions normally varies from 2.18 to 8.65 cm/s [23], [26], [28], [29], [36], [37], we assumed that the longest time it takes for EHG to transmit from each electrode to its neighbor is 1 s. Therefore, the depth of context-tree was set to $D = 8$. In this way, the past activity of D samples of any derivative sequence X^n included $\{x_{n-30}, x_{n-60}, x_{n-90}, x_{n-120}, x_{n-150}, x_{n-180}, x_{n-210}, x_{n-240}\}$, assuming that the EHG signal depends on within 1.2 s of past activity.

C. EHG propagation terminal zone identification algorithm

Propagation terminal zone (PTZ) of EHG was defined in this study as the location in the plane of uterus towards which the information flows. We proposed to investigate the PTZ of EHG rather than the detailed direction of EHG propagation, since the electrodes used for EHG recording in this study cannot cover the whole region of uterus.

The identification algorithm was proposed, specifically, for electrode configuration of M-by-N matrix ($M \geq 3$, $N \geq 3$). Therefore, each electrode has at most 8 neighbors. The DI rate between each pair of neighboring channels was estimated using the DI estimator (3). The flow between channel i and j was defined to be inward to channel i if $\Theta(j \to i) = \overline{I}(j \to i) - \overline{I}(i \to j)$ is larger than zero. Hence, the significance of surround-inward flow of causal information towards electrode i can be calculated by

$$\alpha(i) = \frac{1}{8}\left(\frac{1}{N_s}\sum_{k=1}^{N_s}\sum_{j\in A_i}\left(\frac{1}{2}+\frac{\Theta(j\rightarrow i)}{2|\Theta(j\rightarrow i)|}\right)+\frac{1}{2}\times(8-n_r)\right), \tag{4}$$

where N_s is the number of EHG segments used for the analysis, A_i is the aggregate consisting of all neighboring electrodes of i and n_r is the number of elements in A_i. The additional fictitious electrodes with equal potential of inward and outward flow were introduced so as to have relatively fair surroundings of each electrode. According to the values of α of $M \times N$ electrodes, the PTZ was finally be determined by the position of electrode corresponding to the largest value of α.

III. Results

There were recordings from 11 participants where more than or equal to 20 identified UC-associated TOCO peaks were identified and agreed by the two clinicians. These recordings were all collected during pregnancy.

The PTZ identification map was obtained by estimating the significance of surround-inward flow of information of each channel using the estimator α in (4). An example of the PTZ identification map for participant $ice021$ is shown in Fig. 2. The 4×4 grids in the map correspond to the channels in 4×4 electrode matrix with the color representing the value of α. The highest value was observed at channel 11, which illustrates that the PTZ of EHG during UC for participant $ice021$ is indicated by the position of electrode 11. A relatively high value can also be observed at channel 10 in Fig. 2. Table. I summarizes the electrode corresponding to PTZ of EHG estimated by our proposed algorithm for each participant. For 9 out of 11 participants in Table I, the determined PTZ electrodes are along the third column of matrix (electrodes 9 to 12). Among them, 5 women have their estimated PTZ of EHG at electrodes 10 or 11. Besides, the PTZ electrodes estimated for two women are electrodes 5 and 6. Our results illustrate that the channels along the third column of electrode matrix, especially the channels in the center of this column, are more likely to contain most significant surround-inward flow of information.

TABLE I

PTZ electrodes identified by the proposed method across participants

Participant ID	PTZ electrode
ice007	5
ice008	12
ice010	11
ice012	12
ice013	9
ice019	12
ice021	11
ice032	11
ice036	6
ice039	10
ice040	10

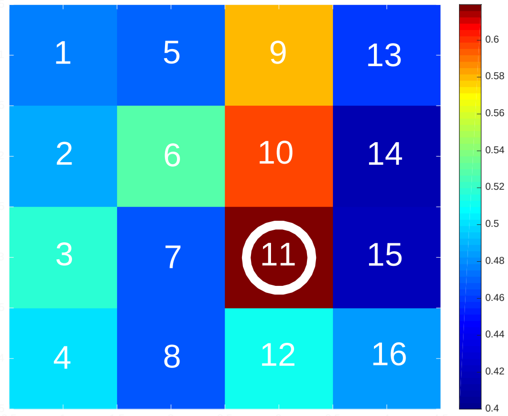

Fig. 2. Example of PTZ identification map obtained by applying the proposed method for participant $ice021$. The number represents the corresponding electrode. The color of the grid represents the value of α for the channel in corresponding position. The identified PTZ is marked by a circle.

IV. Discussion and Conclusions

This study investigated UC propagation via identifying the location towards which the EHG propagates during UCs for pregnant women. The proposed method is based on the estimation of DI which infers causal interactions between EHG channels. Intuitively, activity at the PTZ electrode is driven by the activity at the other electrodes via causal interactions. The PTZ is thus expected to be the destination of UCs, where there are strongest incoming causal connections. Instead of estimating the detailed direction (*i.e.* sources, paths and destinations) of EHG propagation, which requires the electrodes to cover the whole uterus, we focused on determining just the terminal of the flow within the area of electrode matrix. The proposed method is useful to estimate the direction of EHG propagation especially when only part of uterus is covered for data recording, which is of great importance to induce as little discomfort to the pregnant women as possible.

Our results illustrate that the PTZ electrodes are in the third column of matrix for more than 81.8% participants, indicating that during pregnancy UCs, EHG propagates to the medial axis of the uterus within the estimated area (the middle part of uterus). Five participants are shown to have their PTZ electrodes in the middle of the third column, indicating a great possibility that the flow in this area is inward to the center, specifically, half way between the uterine fundus and pubic symphysis along the medial axis of the uterus. Our results are not in contradiction to the results of most previous studies, which demonstrate that the electrical activity of UCs can originate anywhere on the uterus and the EHG signals propagate in different directions [27], [37], [38]. Instead, the propagation towards the center of uterus plane indicates that there could be more than one sources. The PTZ electrodes estimated for four women are in the third column, but not in the middle of the third column. A possible reason could be that, to keep away from the navel, the electrode matrix was displaced up or down, but not exactly on the desired position [30]. Likewise, physiological diversity (*e.g.* different placental position) and observational error can also result in the deviation of matrix position, which makes the estimated PTZ away from the expected region. Although, the PTZ electrodes estimated for two women (participant $ice007$ and participant $ice036$) are not in the third column of matrix, they are nearby.

Furthermore, it is worth noting that as described in Section II-B, most of the parameters involved in the estimation of DI were set based on theoretical rationality. The optimization will be considered in future study regarding the length of windows, the way of quantization and some other parameters.

In conclusion, this study has proposed a novel method to analyze the terminal zone of EHG propagation during UCs. The investigation on experimental data illustrated a specific location towards which the EHG within the middle part of uterus is most likely to propagate during UCs, allowing us to better understand the EHG propagation during normal contractions.

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