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Decrement of uterine myometrial burst duration as a correlate to active labor: A Hilbert phase approach

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Abstract

We propose a novel approach based on Hilbert phase to identify the burst in the uterine myometrial activity. We apply this approach to 24 serial magnetomyographic signals recorded from four pregnant women using a 151 SQUID array system. The bursts identified with this approach are evaluated for duration and are correlated with the gestational age. In all four subjects, we find a decrease in the duration of burst as the subject approaches active labor. As was shown in animal studies, this result indicates a faster conduction time between the muscle cells which activate a larger number of muscle units in a synchronous manner.

I. INTRODUCTION

In the early stages of pregnancy the uterine myometrial bursts are of low amplitude and infrequent in nature. At term gestation and during labor, bursts become more frequent and have a higher amplitude which correlates well with the large change in the uterine pressure [1]. The contractile activity of the uterus results from the excitation and propagation of electrical activity. This activity arises from the generation and transmission of action potentials in the uterine muscle. These action potentials occur in groups referred to as burst. It has been shown that each contraction is accompanied by a burst of action potentials. The uterine myometrium consists of smooth muscles fibers that are arranged in overlapping

tissue-like bands, however the exact arrangement is a highly debated topic [2]. Like cardiac cells, uterine myometrial cells can generate either their own impulses or can be excited by the action potentials propagated from the other neighboring cells. The spontaneous oscillations in the membrane potential of the autonomously active pacemaker cells lead to the generation of an action potential burst when the threshold of firing is reached because they are coupled by electronic synapses called gap junctions. It has been shown that the gap junctions disappear within 24 hours after delivery [3, 4]. The increase in the gap junction number and their electrical conduction provides better coupling between the cells resulting in synchronization and coordination of the contractile events of the various myometrial regions in the uterus. Animal studies have shown that prior to the onset of true labor, the duration of the burst decreases simultaneously with the increase in the gap junction [5]. In this work we study the decrement in the duration of the burst as the subject approaches active labor. The first step towards this approach is to identify the myometrial burst activity.

Identification of uterine contraction (burst) in the physiological signals, namely, electro/magnetomyograms (E/MMG) has been attempted using different methods ranging from a simple zero-crossing (ZC) [6, 7] approach to a more complex wavelet transform (WT) technique [8]. Both approaches have been applied to multi-sensor signals. In [7] the authors use ZC approach followed by the K-means clustering technique (always requesting for three clusters) to distinguish contractions from background activity; in [8] the WT approach is followed by the affinity propagation (AP) clustering technique [9] to distinguish contractions from background activity. While the ZC approach lacks threshold detection to distinguish contractions from background activity, the WT approach relies on the signals from multiple sensors to identify the contractions. Thus, both approaches have limitations in identifying contractions at a single sensor level. A time-frequency analysis (TFA) can also be used to identify the burst locations, however, TFA is sensitive to the amplitude modulation of the signal and hence bursts of low amplitude cannot be identified reliably. Here we propose a novel Hilbert phase approach to identify the occurrence of the burst. To this end we quantify the burst duration and study its variation with gestational age.

To date, several different techniques have been developed to measure uterine contractions. The most commonly used clinical approaches are the intrauterine pressure catheter (IUPC) and tocography (TOCO) [11]. The IUPC is an invasive method that measures the intrauterine pressure via a catheter [12]. A change in pressure inside the uterus is reflected at the tip of the transducer in the catheter. The TOCO is the most common non-invasive technique used to measure the mechanical deflections produced by the uterine contractions. The TOCO technique is widely used by physicians as it is simple and almost risk free to the mother and the fetus. The major drawback of this instrument is the susceptibility to maternal motion artifacts. While, IUPC is more reliable and accurate than TOCO, it is an invasive procedure that requires the rupture of the amniotic membranes, thus limiting its use to patients in whom delivery is necessary. Due to the poor predictive power of the TOCO and the invasive nature of IUPC, neither technique has been beneficial in the prediction of preterm labor or the diagnosis of true labor at term. Currently two methods are employed to record the physiological activity of uterine contractions, (i) EMG, recorded by electrodes attached to the abdomen and (ii) MMG, based on the recording of the magnetic fields that correspond to electrical fields. These techniques measure the electrical/magnetic activity on the surface of the maternal abdomen, which is a result of a sequence of bursts or groups of action potentials that are generated and propagated in the uterine muscle. Garfield *et al* performed simultaneous recording of the EMG activity directly from the uterus and the abdominal surface of rats [13] and showed that the signals recorded from the abdominal surface correspond to those generated in the uterus, suggesting that similar techniques can be used in humans. The recording of the EMG activity from the human uterus using abdominal electrodes was also reported [14]. EMG has a high temporal resolution. However,

because of the differences in the conductivities of tissue layers, the EMG signals are filtered during their propagation to the surface of the abdomen. The first MMG recordings of spontaneous uterine activity were reported by Eswaran *et al.* [10]. The MMG recordings have important properties: (i) independency on tissue conductivity (ii) detection of the signal without making any electrical contact with the body, and (ii) are reference free, which ensures that each sensor mainly records localized sources.

II. METHODOLOGY

A. Data acquisition and preprocessing

We studied a total of 24 magnetomyographic (MMG) signals recorded using a 151 SQUID array system [10] from four pregnant women ranging in gestational age from 36 to 40 weeks. This study is approved by the local Institutional Review board and all the subjects have given the written consent to participate in the study. The data is sampled at 250 Hz for a period of 20 minutes and for the subsequent analysis the data was down-sampled to 25 Hz. To attenuate the interfering cardiac signals we bandpass filter the data between 0.35 and 1 Hz using Butterworth filter with zero-phase distortion. The low frequency components 0-0.35 Hz are discarded to avoid the interferences from the maternal breathing and movement artifacts.

B. Hilbert Phase based burst detection algorithm

For a uniformly sampled signal $x(t)$, Hilbert transform $h(t)$ is defined through the following convolution integral:

$$h(t) = \frac{1}{\pi} P.V. \int_{-\infty}^{\infty} \frac{x(\tau)}{t - \tau} d\tau,$$

where P.V. denotes Cauchy's Principle Value. Basically this integral introduces a phase shift of -90° to the signal $x(t)$. The signal together with its Hilbert transform can be represented as a complex-value analytic function $a(n)$ as follows: $a(n) = x(n) + i \cdot h(n)$, where $i = \sqrt{-1}$ and $t = n/sf$, sf is the sample frequency in Hertz. All the calculations reported in this work are done using Matlab software (Mathworks Inc. Natick, MA, USA) and the "hilbert" function in this software directly provides $a(n)$. For the complex-value function $a(n)$, the (Hilbert) phase is defined as $\phi(n) = \tan^{-1}\{h(n)/x(n)\}$ and $\phi(n)$ exhibits slips when the magnitude of the successive difference exceeds π . We define the time difference between successive phase slips as $\Delta\tau(i) = \tau_{i+1} - \tau_i$. A histogram of $\Delta\tau$ for periodic signals will have a δ -distribution with the peak centered at the periodicity of the signal and with the amplitude equal to number of such cycles in the signals. Thus, spectral properties can be studied using $\Delta\tau$ and this has been attempted in an earlier work [15] to study spectral content of the atmospheric variables. In the recent work we have localized the spontaneous fetal brain signals by studying the standard deviation of the inter-slip intervals ($\sigma(\Delta\tau)$, where $\sigma(\cdot)$ denotes the standard deviation) [16].

In order to identify the burst in a single sensor, we choose magnetic signals in a 30 sec window and compute $\sigma(\Delta\tau)$ and continue this procedure to the rest of the data in a sliding window of 5 sec. We repeat this analysis for all the 151 sensors. As the contractile burst is a low frequency component, it will have a higher $\sigma(\Delta\tau)$ compared to the background activity and we use this property to identify the bursts. Further, it may appear possible to identify the bursts by computing the average frequency of the unwrapped (Hilbert) phases. However, in a given inspection window if the percentage of burst (duration) is small compared to the window duration then the frequency of the Hilbert phase will quantify the background

activity rather than the burst itself and hence this approach cannot be used reliably to identify the bursts. To locate the burst we follow these steps:

- Compute the magnitude of the Hilbert transform of the MMG signal.
- The time windows corresponding to the local minima of $\sigma(\Delta\tau)$ are located.
- The median value of the data corresponding to the time windows are calculated.
- A baseline is defined as the mean of all the median values.
- The signal content above the baseline is defined as the burst and the duration of this burst is studied as across gestational age.

III. RESULTS AND DISCUSSIONS

In Figure 1 we present the burst identified using the novel Hilbert phase approach for a serial MMG data recorded on five different gestational days from a typical subject (subject 3) until the subject reached the active labor. We set the cervical dilation greater than 3 cm as a criterion to define the active labor and choose the data with highest signal to noise ratio (SNR) for further analysis. This is selected by studying the variance of the phase slip metric $\sigma(\Delta\tau)$ computed in 30 sec windows with a slide of 5 sec. $\sigma(\Delta\tau)$ is not a typically used metric to estimate SNR. In our earlier works, we have shown that the phase slip metric can be used to distinguish the sensors containing the fetal brain signal embedded in 151-SQUID sensors [15, 17]. Further, using this metric we could successfully identify the spontaneous brain patterns of the fetuses and newborns [18]. Based on these two preliminary works, we believe that this approach can be used as an equivalent to SNR as it distinguishes the signal of interest from the background activity. A sensor that contains contractile activity with high SNR, interspersed with background activity will display a larger variance in $\sigma(\Delta\tau)$ compared to sensors that have low-contraction activity or background activity. Hence we choose to present the sensor with the highest $\sigma(\Delta\tau)$ (SNR) in Figure 1 from all the five data sets from this subject. The day on which subject reached active labor was chosen as a reference (zeroth day) and the day on which the MMG study is conducted is calculated backwards from this reference day. It is clear from Figure 1 that in earlier gestation, the bursts are long and small in amplitude. However, as the subject approaches active labor the bursts become more regular with high amplitude. We compute the duration of the burst and study its variation with gestation age. For this purpose we consider the top five sensors based on the variance of $\sigma(\Delta\tau)$. In Figure 2 we present the variation of the burst duration as a function of the gestational days. For each subject the mean $\pm$ standard deviation is shown for the top five sensors with highest SNR (decreases from top to bottom). It is clear from Figure 2 for subjects 1, 2 and 3 that the burst duration decreases as they approach active labor. In subject 3, for whom the data on the day of active labor was also available, a negative trend in the duration of the burst is seen in almost all the sensors (top to bottom) indicating that the majority of the sensors display the same MMG characteristics. This is in agreement with the earlier study that many active regions evolve prior to the onset of labor [5]. Though in subject 4, the negative trend is low (close to zero), the durations of the bursts is low compared to the other subjects indicating that the uterus of this subject is already in the active phase for labor.

IV. CONCLUSION

In previous studies we have shown the feasibility of measuring MMG activity of the uterine smooth muscle [10]. Further an increase in the amplitude of the MMG signals is noted for the subjects in active labor (with cervical dilation greater than 3 cm) compared to subjects that had contractions but not in active labor [19]. In this study we have identified the uterine

myometrial burst activity using a novel Hilbert phase approach and shown that there is a decrement in the duration of the burst as the subject approaches active labor. This result is in agreement with the animal study [5] that has demonstrated an increase in the gap junction with the simultaneous occurrence of bursts of short duration and with large amplitude. Based on our results we can conclude that the muscle cells in different parts of the uterus work in a coordinated manner to expel the fetus out the maternal body. Our preliminary results (three out of four subjects) seem to correlate reasonably well with the clinical outcome. In future work this approach will be tested on a large population of data to validate this correlation. Further, other parameters such as inter-burst intervals, frequency of the bursts and clinical parameter such as gravida (primi/multi) will also be examined for their potency in predicting active labor. In addition, we also plan to perform synchronization analysis to understand this coordinated behavior of the uterine smooth muscle activity.

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Fig. 1.

Burst activity identified in five serial MMG data recorded on different gestational days from a typical subject (subject 3). The sensor that exhibited highest SNR is shown in all the days (see text for details). The days on which the recordings are performed are given as title in each graph (see text for details). The MMG activity is shown in pico Tesla (pT) units and the time is in second (sec). For the sake of clarity the scaling of the y-axis is different for each day. We have discarded 20 sec of data in the beginning and end of the data to avoid the ripple effects caused by the filter.

Fig. 2.

The variation of duration of the bursts identified by the novel Hilbert phase approach as a function of the gestational days. The mean plus one standard deviation of the burst duration is shown for all the four subjects. For each subject the burst durations are shown from top five sensors based on the highest SNR (top to bottom). The unit of burst duration is sec. For the sake of clarity the axes are shown in different ranges. The sensors that showed largest negative trend are displayed as inset. The unit of trend is sec/day.