SPATIAL TEMPORAL ANALYSIS OF UTERINE SMOOTH MUSCLE ACTIVITY

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Abstract: We performed recording of the magnetic fields (Magnetomyography - MMG) corresponding to the electrical activity of the uterine smooth muscle with a device called SARA, (SQUID Array for Reproductive Assessment). Past studies suggest the uterus passes through a preparatory process before entering labor and resulting in delivery of the fetus. But the electrophysiological mechanism of this process is not completely understood. We propose five parameters that will allow us quantify the characteristics of the uterine MMG signal obtained from 151 sensors spread over the pregnant abdomen. In summary, we believe that spatial-temporal analysis mapping of uterine activity will help us better understand the process of labor.

Introduction

The uterus is normally able to accomplish the remarkable task of maintaining an environment which suppresses uterine contractile activity during the development of the fetus. Close to the time of the delivery, the uterus initiates and coordinates the individual firing of myometrial cells to produce organized contractions causing the expulsion of the fetus from the mother's body. The contractile activity of the uterus results from the excitation and propagation of electrical activity. The electrical activity arises from the generation and transmission of action potentials in the uterine muscle. These action potentials in the uterine muscle occur in groups referred to as a burst. It has been shown that each contraction is accompanied by a burst of action potentials. The frequency of the action potential within a burst, the duration of the burst and total number of simultaneously active cells are directly related to the frequency, amplitude and duration of a contraction.

The uterine myometrium consists of smooth muscle fibers that are arranged in overlapping tissue-like bands, the exact arrangement is a highly debated topic [1]. Like cardiac cells, uterine myometrial cells can generate either their own impulses - pacemaker cells- or can be excited by the action potentials propagated from the other neighboring cells - pacefollower cells. But unlike cardiac cells, each myometrial cell can alternately act as a pacemaker or a pacefollower. In other words, there is no evidence of the existence of a fixed anatomic pacemaker area on the uterine muscle [1][2]. 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. The electrical activity arising from these pacemaker cells excites the neighboring cells, because they are coupled by electronic synapses called gap junctions. It is believed that the action potential burst can originate from any uterine cell, thus the pacemaker site can shift from one contraction to another [1][2].

Electromyography studies performed by Garfield et al show that there is infrequent and unsynchronized low uterine electrical activity throughout most of the pregnancy [3][4]. They have shown the gap junctions are sparse throughout pregnancy but increase during delivery in various species. Also, it was observed that these gap junctions disappeared within 24 hours of delivery. The increase in the gap junction number and their electrical transmission provides better coupling between the cells resulting in synchronization and coordination of the contractile events of the various myometrial regions in the uterus. Thus the efficiency of contractions leading to labor depends on the synchronous burst activity over a large area of the uterus. Therefore it is important to determine the extent of propagation throughout the multi-cellular uterine muscle bundle. Since the propagation of these uterine contractions can be in both longitudinal and transverse direction we need to determine the propagation characteristics over the entire maternal abdomen while performing surface recordings. We believe that information regarding the spatial-temporal activation of the uterus may be predictive of onset of labor leading to the delivery of the fetus. Thus, a complete spatial-temporal mapping of uterine activity throughout pregnancy is a key parameter that will improve the understanding of the uterine contraction mechanism. In this communication we present five parameters that could quantify the uterine MMG signal characteristics.

ISSN: 1727-1983 © 2005 IFMBE

Materials and Methods

The MMG recordings were performed using SARA system that consists of 151 primary magnetic sensors spaced 3cm apart over an area of 850 cm^2 [5][6]. SARA is a stationary, floor-mounted instrument where the mother sits and leans her abdomen against an anatomically shaped sensing surface (Fig 1). This design is inherently safe. The mother is comfortable, and can gain easy access to or dismount from the system.

Figure 1

(a) : Mother positioned on the SARA system

(b) A cut-our view of the sensor lay-out.

The sensors are arranged in a concave array covering the maternal abdomen. This array surface is curved to match the shape of the pregnant abdomen. The mother simply sits and leans forward slightly against the smooth surface of the array allowing the SQUID sensors to receive signals from the entire maternal abdomen. SARA, is installed in a magnetically shielded room next to the labor and delivery unit. The magnetic shielded room is necessary to reduce external magnetic fields, which interfere with the biomagnetic field generated by human organs. The SARA system was built for the study of the fetal neurological system with the support of a grant provided by the National Institute of Neurological Disease and Stroke (NINDS) division of NIH.

Fifty patients ranging in gestational ages between 28 and 41 weeks had 8 minutes of recording sessions each. After obtaining a written consent, the mothers were asked to sit comfortably and lean forward on to the sensor array. The mothers were asked to raise their finger for the duration of each perceived contraction. Based on this information, the operator synchronized the beginning and end of the contraction by marking these time points in the record. The recordings were made at a sampling rate of 250 Hz. The data was then down-sampled to 25 Hz and post-processed with a bandpass filter (0.05 - 1 Hz) for further analysis. In order to localize the areas of activation over the uterus during a contraction, a contour map of the magnetic field distribution was plotted. The pattern of the field distribution helps in determining the area of activity over the uterus thus allowing for precise localization of the source of the MMG activity.

To identify and characterize the regional activity within the uterus, we chose to look at five tracking parameters to define uterine activity - (1) Frequency (F) of electrophysiological burst activity, (2) Peak Power (PP) - to quantify the intensity of the magnetic field related to electrophysiological activity, (3) Percentage of Sensors Active –(PSA) to determine the spread of activity over the uterus (4) Regions of Activity (RA) – the number of isolated regions active over the uterus (5) Synchronization of Activity.

The frequency and peak power were obtained by using the standard spectra analysis procedure. By performing spectral analysis on an MMG burst activity we can obtain the relative strength (or the energy content) of the components that constitute the burst as a function of frequency. The spectral plots were obtained using the standard Fast Fourier Transform (FFT) technique. The synchronization and de-coherence indices between two adjacent sensor channels were computed after taking the Hilbert transform of the data. The synchronization between a pair of channel was inferred from a statistical tendency to maintain a nearly constant phase difference over a given period of time even though the analytic phase of each channel may change markedly during that time frame. The Hilbert transform was applied on the pairs of magnetic field traces (60 second length) with a sliding window of 10 sec duration which is long enough to cover at least one cycle of the lowest frequency of interest (0.1 Hz). The analysis was repeated by stepping the window at 10 sec intervals. The synchronization and de-coherence indexes were computed for each pair of magnetic field traces. The RMS (root mean square) magnetic field for each channel in the 10 sec windows was also computed.

Results

Figure 2 shows a sample uterine burst activity interspersed by quite periods. Figure 2 (top) also shows the areas of activity during a contractile period. Spectral Analysis of MMG signals revealed that peak power ranged from 1 to 10 pT with peaks at two frequency ranges of 0.15 - 0.2 Hz and 0.3 – 0.5 Hz. Figure 3 shows the PSA and regions of activation. The top part of the figure shows the number of sensors active (dark circles) over the pregnant abdomen during the non-contractile. It can be seen there are two isolated regions of activity. The bottom part of the figure depicts a contractile period where the activation is spread over large area. Higher sensor count implies increase in the spread of electrical activity. The spread of the activity relates to improved propagation of the electrophysiological activity leading to successful delivery of the fetus. The region of isolated activity ranged from 1 to 3. PSA was <33% on the first day of recordings implying that only 1/3 of the recording area was magnetically active over the abdomen. The number of serial recordings per patient ranged from one to maximum of 19. Most of the patients who were contracting had at least 50% percent of the sensors (PSA). 90% of patients with increased PP and /or PSA delivered within four days of their last examination where a 50% increase in PP or PSA was considered significant.

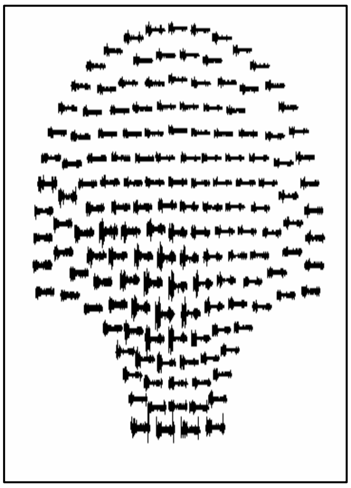
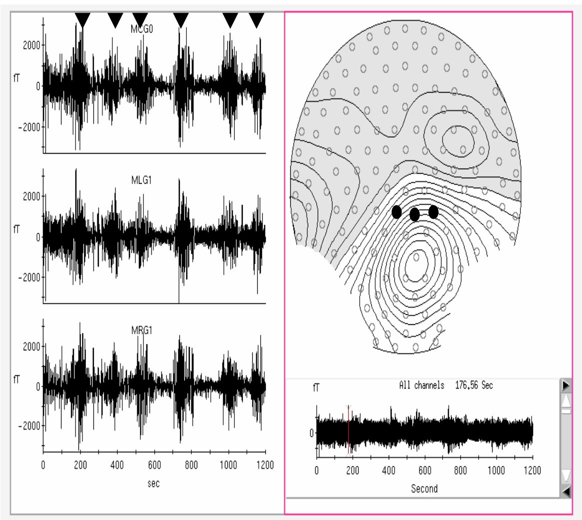


Figure 2 ***(top)*** *Uterine MMG signals recordings from 151 channels with strong uterine activity seen in the lower left side of the abdomen.* ***(bottom)*** *The expanded view of the MMG activity recorded from the three sensors under the region of maximum activity (left), localized by obtaining a contour map of magnetic field distribution during a contraction at a time point of 176 sec.*



The middle row of Figure 4 shows 2-D contour plots of the RMS magnetic fields and the bottom row shows the synchronization indices over the front of uterine area. Spatial patterns of the synchronization

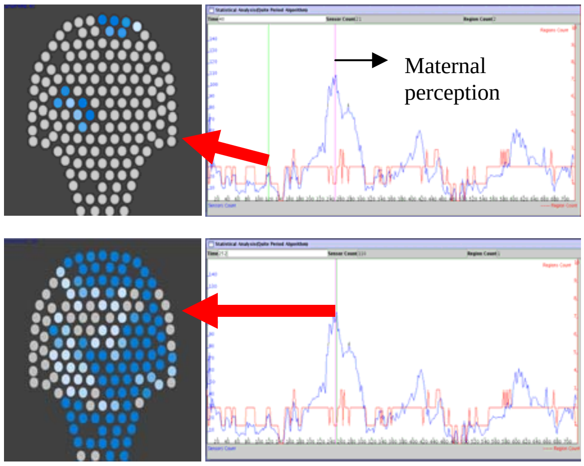


Figure 3 *The number of sensors active (dark circles) showing spread of activity over the pregnant abdomen during the non-contractile* ***(top)*** *and contractile period* ***(bottom).*** *Higher sensor count implies increase in the spread of electrical activity.*

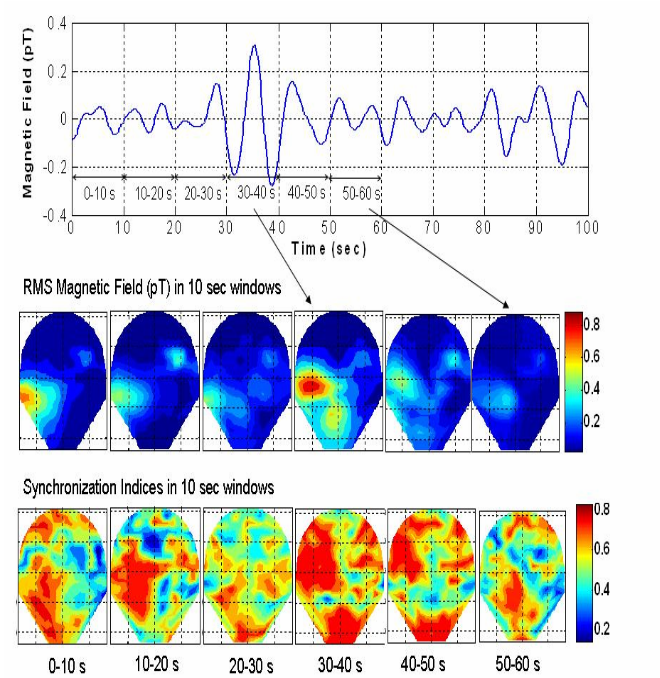


Figure 4 ***(top):*** *A sample MMG burst from one channel.*
(middle) *2-D contour plots of the RMS magnetic fields. Blue color shows minimal activity. The red and yellow colors in 30-40 s window shows the dipolar activity of magnetic field representing the source of that activation.*
(bottom) *The synchronization indices over the front of uterine area. Spatial patterns of the synchronization indices have a good correlation with the RMS magnetic field patterns. The red areas in the plots depict higher synchronization.*

indices have a good correlation with the RMS magnetic field patterns. This correlation is observable in each 10 sec window. These 2-D plots covers one uterine contraction cycle. The red areas in the plots depict higher synchronization. These plots show that during contraction larger areas of uterine have higher levels of synchronization as compared to the 10 sec window before and after the contraction.

ISSN: 1727-1983

Discussion

The SARA System can record the magnetic field corresponding to the electrical activity of uterine contraction and provide requisite spatial-temporal information. The spatial-temporal information provided by the 151 channels will provide much more information about the contractile nature of the uterus than has previously been possible to obtain. Past studies by Garfield et al [3], using abdominal electrodes have also reported that the uterus goes through a preparatory stage before onset of labor and there is an increased electrical activity during that period. They have recently attempted to characterize and quantify the electrical preparedness of the uterus during which the transition occurs. Though this is also a non-invasive approach, the disadvantage of using the transabdominal electromyography technique is that electrical signals reaching the abdominal surface are highly dependent on tissue conductivity. This technique imposes a restriction in performing any simple analysis on acquired signals as there is a high intra-subject variability in the signal strength and noise based on the variance in conductivity at the skin-electrode interface. Also, to maximize the signal strength, extra care is required to prepare the electrode sites in order to minimize the skin impedance.

In contrast, transabdominal magnetomyographic recordings are far less dependent on tissue conductivity. There is no need to prepare the measuring site to reduce the skin impedance and the patient simply leans forward with her abdomen overlaying the array of magnetic sensors. This study shows that this system is capable of localizing the area of activation over the uterus during a contraction. This will allows us explore the origin and propagation of uterine contraction despite the shifting of the pacemaker site from one contraction to another. We can localize the pacemaker by mapping the magnetic field distribution and quantify the spread by obtaining the percent of sensors active during each contraction with sensors spread over the entire maternal abdomen. Using this information, in further studies it will be possible to test the hypothesis that during most of pregnancy uterus is spontaneously active but because of limited propagation of the action potentials only small areas of myometrium is activated. Whereas closer to active labor, gap junction appear and increased number of myometrial cells are activated resulting increase in the spread of electrical activity over the uterus. This will also confirm that the uterus goes through a preparatory phase before labor starts.

Conclusions

Complete spatial-temporal mapping of uterine activity throughout pregnancy is a key parameter in the understanding of the uterine contraction mechanism and is not easily achievable by any other technique. The detailed spatial-temporal resolution of the SARA instrument can be used to determine the regions of localized activation, propagation velocity and direction, and the spread of activity as a function of distance. The five tracking parameters including the frequency, peak power, percent of sensors active and the isolated regions of activity could be used to track the evolution of labor during pregnancy. Further serial MMG recordings on pregnant patients with 151 multipoint detection system, should help us observe these changes by tracking the propagation characteristics including the extent of propagation. This data would be used to define the physiological steps leading up to organized uterine contractions and thus forming the basis for the development of a methodology to accurately predict the onset of active labor. This ability would be of great clinical benefit for the management of the term patient and especially for the management of patients at high risk for premature delivery. Through more detailed and precise information regarding the initiation and propagation of activity in the human uterus it is hoped that new, more effective approaches can be developed for the suppression of preterm labor and also, for the induction of labor.

Acknowledgments This project was partially supported by a NIH grant 5R33 EB00978-01 (National Institutes of Biomedical Imaging and Bioengineering). We would like to acknowledge the support of Dr. Coskun Bayrak and his group at University of Arkansas at Little Rock in developing some of the analysis tools.

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ISSN: 1727-1983 © 2005 IFMBE