Towards improving uterine electrical activity modeling and electrohysterography: ultrasonic quantification of uterine movements during labor

HINKE DE LAU¹, CHIARA RABOTTI², NICOLE HAAZEN², S. GUID OEI¹ & MASSIMO MISCHI²

¹Department of Obstetrics and Gynecology, Máxima Medical Center, Veldhoven and ²Department of Electrical Engineering, University of Technology Eindhoven, Eindhoven, the Netherlands

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Abstract
The electrohysterogram is a potential new tool for diagnosing preterm labor. Parameters from the electrohysterogram may be influenced by uterine movement. An observational study was performed quantifying uterine movement during labor as a step towards improving electrohysterogram analysis for predicting preterm labor. The uterine wall was continuously tracked by ultrasound imaging during first stage of labor while an accelerometer recorded external abdominal accelerations in six women. A cyclic cranial–caudal movement of the uterine wall, caused by maternal respiration, was observed. This is reported and quantified for the first time. Average frequency, amplitude, and peak speed were 0.27 ± 0.07 Hz, 0.68 ± 0.84 cm, and 1.04 ± 1.20 cm/s, respectively. The accelerometer signal correlated with uterine movement and therefore can possibly provide a reference for removing movement-induced artifacts. There is a need to model and measure the effect of uterine movement on the electrohysterogram parameters and make measurements more robust to movement artifacts.

Abbreviations: A(t), amplitude of the measured abdominal acceleration; BioMod UE-PTL, biophysical modeling of the uterine electromyogram for understanding and preventing preterm labor; EHG, electrohysterogram; U(t), amplitude of the uterine movement; US, ultrasound.

Introduction
The electrohysterogram (EHG) is a non-invasive measurement of the electrical activity underlying uterine contractions. The EHG can be measured by electrodes placed on the abdomen; each electrode records the electrical activity of the myometrium underneath the electrode. Previous publications have demonstrated that the EHG is a potential new diagnostic tool for monitoring labor, discriminating between physiological and pathological contractions and thereby supporting timely treatment of preterm labor (1–5).

Unfortunately, introduction of diagnostic tools into clinical practice based on the EHG is hampered by a lack of understanding of the link between the action potentials initiating (preterm) labor and the EHG signal recorded on the skin surface. The propagation of action potentials originating in myometrial cells and the resulting EHG signal measured on the skin surface builds on several complex processes as the signal propagates from cell to cell within the myometrium (6) and through the tissue layers underneath the skin (7). Furthermore, tissue layers can vary in thickness and also move mutually. All these factors affect the
measured EHG signal and make its interpretation challenging.

The international BioMod UE-PTL project [Biophysical modeling of the uterine electromyogram for understanding and preventing preterm labor (8)] focuses on multi-scale modeling to understand the link between the electrical activity at the cell level and the EHG signal recorded on the skin (9). The ultimate objective is to obtain the necessary knowledge for a new EHG-based tool for the diagnosis of preterm labor.

As part of the BioMod UE-PTL project, this study focuses, for the first time, on continuous measurement of the mechanical activity of the myometrium by abdominal ultrasound (US). Our primary objective was to observe myometrial changes and movements during labor as a first step to improve the interpretation of the EHG signal measured on the skin surface during pregnancy and labor.

**Material and methods**

An observational study was performed. Approval was granted by the local medical ethical board and written informed consent was obtained. The study was conducted according to the principles of the Declaration of Helsinki (59th WMA General Assembly, October 2008). Inclusion criteria were women in the first stage of labor, singleton pregnancy, and a gestational age of at least 37 weeks. Only women with epidural analgesia were included due to the need to remain still in order to obtain high quality US images. The target inclusion size was 10 women. It was not possible to perform a power analysis. The mechanical activity of the myometrium was continuously assessed by abdominal US measurements. An Aloka SSD 100 US scanner (Hitachi Aloka Medical, Tokyo, Japan) was used in B-mode (2D mode) in combination with a 6-MHz abdominal convex probe. The US probe was placed perpendicular to the skin. A position was chosen just below the umbilicus and close to the midline of the abdomen in order to obtain optimal contrast between the uterine wall and the surrounding tissues and to measure the myometrium underneath our standard position for EHG electrode placement (10). Both sagittal and transversal US recordings were obtained for a minimum of three contractions for each woman. A tocodynamometer was positioned above the umbilicus to record contractions and provide a reference by the standard clinical monitoring method. Finally, a 3D accelerometer was placed on the maternal abdomen close to the US probe, enabling the measurement of the accelerations of the abdominal surface, thereby indirectly capturing movement of the abdominal surface in three directions, x, y, and z. The B-Mode US recordings, digitized at 25 frames/s, the tocodynamometer, and the measured accelerations, were stored on a computer for further analysis.

Uterine movement was analyzed with the following procedure. US data were first visually inspected to exclude frames that contained out-of-plane probe movements. To estimate uterine movement, selected portions of the US image were followed over time using a speckle tracking algorithm based on 2D cross-correlation [see (11) for a more detailed description]. Based on the assumption that subcutaneous tissue does not move relative to the skin, the displacement of both uterus and subcutaneous tissue were tracked to compensate for small movements of the probe. The speckle tracking algorithm was independently applied to the subcutaneous tissue layer and to the uterine layer. The uterine movement, \( U(t) \), was estimated by subtracting the displacement of the subcutaneous tissue layer from the displacement of the uterus. For each participant the peak frequency and the average amplitude of the uterine movement were calculated. The peak speed was then derived based on a sinusoidal movement.

The \( z \)-axis, perpendicular to the skin surface, of the 3D accelerometer was used to correlate the amplitude of the measured abdominal acceleration, \( A(t) \), and the amplitude of the uterine movement, \( U(t) \). The correlation between \( A(t) \) and \( U(t) \) was quantified by the maximum of the normalized cross-correlation function, \( \rho \). The correlation between \( A(t) \) and \( U(t) \) was also calculated in the frequency domain. Oscillatory uterine movements were observed in all women, which were considered to be induced by maternal respiration. Therefore band-pass filtering was applied to \( U(t) \) in the frequency band corresponding to respiration frequencies [0.17–0.67 Hz]. The Pearson correlation coefficient, \( r \), between the power density spectra of \( U(t) \) and \( A(t) \) was calculated. The peak frequency of both signals was compared and the Wilcoxon signed-rank test used to test for statistical significance.

**Results**

A total of nine women were enrolled, but three were excluded from analysis: one measurement was stopped at the woman’s request, another was stopped because fetal bradycardia was detected during the measurement and one measurement could not be analyzed because of inadequate US quality. The gestational age ranged from 37\( ^{+5} \) to 40\( ^{+5} \) weeks, the body mass index from 22.0 to 25.6 kg/\( m^2 \) and the cervical dilatation from 2 to 9 cm. Five women were nulliparous and one had a history of a cesarean delivery. After excluding all US segments affected by out-of-plane or large translational movements, 110 min of US recordings were analyzed, with an average of 19 \( \pm \) 7 min per participant.
As shown in Table 1, in all women a cyclic cranial–caudal movement of the uterine wall with respect to the skin was detected in the US data. Based on observation, this movement had a sinusoidal pattern, here simply referred to as uterine movement. The average amplitude of this movement (calculated as the full motion divided by two) showed a high inter-woman variability of 0.03–2.49 cm. In each woman, the average period (duration of one cycle) ranged from 2.7 to 5.3 s, corresponding to oscillation frequencies of 0.19–0.37 Hz and a peak speed of the uterine wall of 0.04–3.60 cm/s. The frequency, amplitude, and speed of the uterine movement, respectively, were on average 0.27±0.07 Hz, 0.68±0.84 cm, and 1.04±1.20 cm/s. Analysis of the correlation between the accelerometer signal amplitude, $A(t)$, and the uterine movement, $U(t)$, showed an average correlation $q = 0.51\pm0.08$. No significant difference ($p < 0.05$) was found in the peak frequency. The correlation coefficient of the power density spectra was $r = 0.85\pm0.06$.

The hypothesis that the uterine movement was due to respiration was confirmed by an additional measurement on a pregnant woman (35 weeks gestational age) who was not in labor and was without epidural analgesia (Figure 1). Similar to the measurements in labor, an accelerometer was placed on the abdomen and the uterine movement was measured by US. When this woman stopped breathing for a short period, uterine movement and abdominal acceleration were no longer detected.

### Discussion

This aim of the present study was to observe the mechanical activity of the uterus during labor, in order to improve the interpretation and measurement of abdominally derived EHG. For the first time, uterine movement was quantified and correlated to abdominal acceleration.

In all the women, a cyclic movement of the uterine wall underneath the abdominal surface was observed in the vertical direction (caudal–cranial). An additional dedicated measurement, in which this vertical movement disappeared when the woman held her breath, confirmed this movement to be caused by maternal respiration. Since this movement was not observed in the tissues above the uterus, i.e. skeletal muscle and subcutaneous tissue, our hypothesis is that the organs lying in the abdominal cavity within the peritoneum, including the uterus, are displaced by the diaphragm during respiration relative to the abdominal layers outside the peritoneum. The observed high inter-patient variability could be due to individual differences in type of breathing: chest or diaphragmatic breathing. Following our hypothesis, diaphragmatic breathing would lead to a higher amplitude of the uterine movement.

The correlation between the uterine movement and the detected acceleration was calculated using the maximum of the normalized cross-correlation, rather than the Pearson correlation coefficient, in order to have a measure of correlation that was independent of the synchronization accuracy between the signals. Although the uterine movement has the same frequency as detected by the accelerometer, the signals have only a modest correlation in the time domain. We deduce that, in this domain, nonlinear effects, presumably in the phase of the equivalent transfer function between the signals, play a dominant role. These effects are likely to result from the complex mechanical system linking abdominal accelerations and uterine movements. A system identification approach should therefore be used to process the signals prior to performing any correlation analysis. This approach is being considered for future research.

The uterine movement due to respiration was present in all women and with a frequency approximately in the frequency range used for EHG analysis (5). Our findings
have important implications for the models currently under development for signal propagation and the interpretation of the abdominally derived EHG (9). First, they imply movement of the signal source; the electrodes of the EHG record the signal at that specific location with a continuously moving myometrium underneath. Therefore, EHG parameters previously proposed for characterization of uterine contractions during pregnancy and for prediction of labor, such as frequency content (5) and conduction velocity (3,4), may be affected by uterine movement induced by respiration. Secondly, abdominal movement can cause measurement artifacts due to variations in the electrode-to-skin contact. The interpretation should therefore be adjusted by taking uterine movement into account. The main question that arises relates to the extent of the influence of respiration on the observed variations in EHG parameters.

Since the EHG propagation properties have been recently suggested as the most promising indicators for preterm labor prediction (8), understanding the effect of uterine movement on the measured EHG conduction velocity would be particularly relevant. In this study, the uterine movement had a peak velocity of 1.04 cm/s. As this value is much smaller than the values of EHG conduction velocity previously reported in the literature, i.e. 4.9–53 cm/s (3,4,6), we infer that the effect of respiration-induced artifacts on the analysis of the EHG conduction velocity is negligible. However, as the mechanism underlying EHG signal propagation is still unclear (4), there is a need to thoroughly understand and quantify the effect of uterine movement on the parameters derived from EHG signal analysis to avoid misinterpretation of clinical results. There is a need to focus on understanding and modeling the effects of the observed uterine movements on the EHG signal, possibly leading to improved methods for EHG analysis that are robust with regard to respiration-induced artifacts (12). Understanding and modeling the link between respiration and EHG is essential for reliable use of the EHG for prediction of preterm labor.

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References
