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Ultrasound analysis of the uterine wall movement for improved electrohysterographic measurement and modeling

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Abstract— **During pregnancy, analysis of the electrohysterogram (EHG), which measures the uterine electrical activity, can provide a fundamental contribution for the assessment of uterine contractions and the diagnosis of preterm labor. However, several aspects concerning uterine physiology and its link with EHG measurements are still unclear. As a consequence, the EHG is not yet part of the clinical practice. There is general consensus that modeling and analysis of the EHG can be improved only by understanding and integrating the main properties of the uterine physiology at different levels, *e.g.*, cellular, tissue, and organ, and of different nature, *e.g.*, electrical, mechanical, and structural. In this study, we use transabdominal ultrasound (US) measurements to investigate the mechanical changes that the uterus undergoes during pregnancy under the effect of contractions. We refer to this measurement as mechanohysterogram. Analysis of the mechanohysterogram highlights, for the first time, two phenomena that can influence EHG signal interpretation, namely, changes in uterine wall thickness during contractions and respiration-induced uterine wall movements. Our results suggest that these phenomena can affect the interpretation of the EHG and should therefore be taken into account for accurate modeling and assessment of the uterine electrical activity.**

I. INTRODUCTION

During pregnancy, early recognition of uterine contractions leading to preterm delivery is crucial for preventing premature birth. Unfortunately, uterine activity assessment is still a major issue for gynecologists. Surface measurement of the uterine electrical activity, referred to as electrohysterography, is promising for accurate assessment of contractions and preterm delivery diagnosis [1].

The electrohysterogram (EHG) records the electrical activity that underlies the mechanical contraction of the uterus. Dedicated methods have been proposed for the extraction of EHG parameters with potential diagnostic value, such as the contraction timing, amplitude, and propagation velocity [2][3]. Recent clinical studies confirmed the added value of the EHG relative to traditional clinical tools [1]. However, some relevant aspects concerning the physiology of contractions and their link to the EHG have not been understood [4]. Furthermore, a solid knowledge of the interferences and artifacts that may affect EHG signal interpretation is still missing and EHG measurements are therefore not standardized [4][5]. In an effort to address these key aspects, a few studies have focussed on developing models of the uterine activity during pregnancy and parturition [6][7][8]. Multiscale modeling of the electrical activity from the generation at the cell level, through its propagation along the muscle cells up to the EHG signal recorded on the skin surface, has given promising results for an improved interpretation of the EHG [9].

There is general agreement on the fact that significant improvements in EHG signal interpretation can be obtained only by understanding and integrating the main properties of the uterine physiology at different levels, *e.g.*, at the cellular, tissue, and organ levels, and of different nature, *e.g.*, electrical, mechanical, and structural [4][9][10]. One of the aspects to consider is that the EHG is a local measurement, *i.e.*, the signal recorded by each electrode represents an average of the electrical activity within the area underneath. Therefore, the mechanical properties of the uterus and of those tissues separating it from the skin surface (the volume conductor) play a role in the generation and interpretation of the EHG signal which is as relevant as the ionic channel behavior at the cell level. All these phenomena should therefore be understood and incorporated in models and measurement methods.

As part of the BioModUE_PTL European project [10], this study focusses on the observation of the mechanical properties of the uterus during pregnancy and during contractions by transabdominal ultrasound (US). We refer to this measurement as mechanohysterogram. The uterine wall is continuously observed by US in six pregnant women with contractions. Uterine movements are detected using a speckle tracking algorithm based on 2D cross-correlation [11]. The effect of uterine movements on the abdominal surface is measured by a 3D accelerometer placed on the abdomen.

Differently from other muscles, the mechanical behavior of the uterus has never been thoroughly characterized. In this study, a preliminary analysis of the mechanohysterogram highlights, for the first time, two aspects that can be potentially crucial for EHG signal modeling and interpretation, namely, changes in uterine wall thickness during contractions and respiration movements. Changes in uterine wall thickness may play an important role in the EHG signal generation and propagation and have been suggested to be related to uterine contraction directionality [12]. Respiration-induced movement artifacts may affect surface EHG recordings. Both phenomena are therefore relevant for EHG modeling and interpretation and are here preliminarily characterized.

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II. METHODOLOGY

A. Dataset

After acquiring written informed consent, six women in the first stage of labor with gestational age between 37 and 40 weeks were enrolled. Approval was obtained by the medical ethical board of the Máxima Medical Center (Veldhoven, the Netherlands). Only patients with epidural analgesia were included because only under the effect of analgesia the subject could remain still while having uterine contractions. The mechanical activity of the myometrium was continuously assessed by transabdominal US measurements. An Aloka SSD 100 US scanner (Hitachi Aloka Medical, Tokyo, Japan) was used in B-mode (2D mode, 25 frames/s) in combination with a 6 MHz abdominal convex probe. The US probe was placed perpendicular to the skin, just below the umbilicus and close to the midline of the abdomen. This position was chosen to obtain optimal contrast between the uterine wall and the surrounding tissues, and to measure the uterus underneath the typical electrode position for EHG recordings [3]. The US scanner was set such that the uterus was fully displayed and in focus. A tocodynamometer, which is the standard clinical tool for uterine contractions monitoring during labor, was positioned above the umbilicus. Finally, a 3D accelerometer was placed on the abdomen close to the US probe, enabling the measurement of the accelerations of the abdominal surface in three directions.

B. Data analysis

An iterative 2D speckle tracking method was used to derive the uterine movement signal, $U(t)$, in both the sagittal as well as in the transversal US image sequence [11]. Visual inspection of the image sequences revealed two main phenomena in the uterine wall: thickness changes during contractions and periodic vertical oscillations. Since these oscillations were independent of uterine contractions, based on their periodicity and direction, they could be ascribed to respiration. Periodic oscillations were visible also in the recorded acceleration signal. After deriving the uterine movement $U(t)$ by speckle tracking and calculation of the acceleration vector magnitude $|A(t)|$, the analysis of $U(t)$ and $|A(t)|$ was further tailored to confirm and characterize respiration-induced phenomena, to measure the correlation between uterine movement and surface accelerations, and to quantify uterine thickness changes during contractions.

1) Speckle tracking: After selection of a region of interest (ROI), speckle tracking estimates the translational displacement between subsequent frames of a kernel, K, of size $M \times N$ pixels within the ROI in the frame f, by searching for a similar pattern in the consecutive frame, $f+1$. To increase speed and accuracy, the search was limited to a subregion of frame $f+1$, referred to as search region, S. Displacement was obtained by maximization of the 2D normalized cross-correlation function NCC$[i,j]$, where (i,j) are the coordinates of the search region in the frame $f+1$. Indicated by I_K the intensity of the kernel, I_S the intensity of the search region, and $\overline{I_K}$ and $\overline{I_S}$ their averages, the NCC is defined by

$$NCC[i,j]=\frac{\sum_{x=1}^{M}\sum_{y=1}^{N}\left(I_K[x,y]-\overline{I_K}\right)\left(I_S[x+i,y+j]-\overline{I_S}\right)}{\sum_{x=1}^{M}\sum_{y=1}^{N}\left(I_K[x,y]-\overline{I_K}\right)^2\sum_{x=1}^{M}\sum_{y=1}^{N}\left(I_S[x+i,y+j]-\overline{I_S}\right)}. \quad (1)$$

The central coordinates of K in the frame $f+1$ are given by $(i+M/2, j+N/2)$ such that $(i,j)=\arg\max\{NCC[i,j]\}$. The speckle size was first estimated for each type of tissue as a lower bound for the Kernel size. The average size of the speckles in B-mode images was estimated by calculating the 2D autocovariance function and deriving the full width at half maximum of the resulting curve [13]. The kernel was updated every 2 frames.

The uterus is separated from the abdominal surface by layers of subcutaneous tissues. Based on the assumption that subcutaneous tissue does not translate during contractions, in order to compensate for small translational movements of the probe and measure uterine movements only, the displacement of both uterus and subcutaneous tissue were tracked. The uterine movement $U(t)$ was eventually estimated by subtracting the displacement estimated in the subcutaneous tissue from that estimated in the uterine ROI. To this end, from the first frame of the US image sequence two ROIs were selected within the subcutaneous tissue and four ROIs within the uterus. The speckle tracking algorithm was then independently applied to all ROIs and the average displacement derived.

2) Respiration-induced movements: In all cases, a cyclic vertical (cranial-caudal) movement of the uterus with respect to the skin was observed. To analyze these movements, $U(t)$ was derived by speckle tracking and analyzed only in the sagittal plane. To test the hypothesis that these cyclic uterine movements are due to respiration, an additional measurement was performed on a pregnant woman, not in labor, who was asked, during the measurement, to hold her breath for two short periods.

Assuming an average frequency of respiration of 0.34 Hz, those frequency components not originating from respiration were filtered-out from $|A(t)|$ and $U(t)$ using a fourth order Butterworth band-pass filter. Cut-off frequencies 0.17 Hz and 0.67 Hz were chosen, based on the fact that respiration in pregnant patients is slightly increased compared to normal respiration rates.

For each patient, the peak frequency and the average amplitude of the measured uterine movement $U(t)$ were calculated. An estimation of uterine wall velocity could then be derived. The correlation between $U(t)$ and $|A(t)|$ was calculated by the maximum, ρ, of the NCC rather than by the Pearson correlation coefficient, in order to have a measure of correlation which was independent of the synchronization between the signals. Furthermore, the Pearson correlation coefficient, r, was calculated between the power density spectra of the acceleration and the uterine movement. To derive this parameter the acceleration signal was not filtered. The peak frequency of $U(t)$ and $|A(t)|$, was also compared.

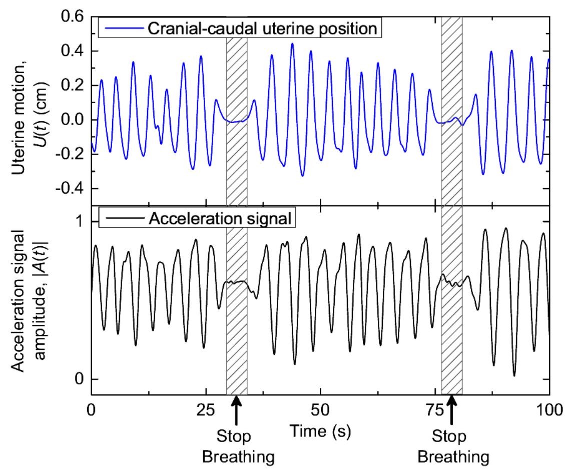

Fig. 1. Cranial-caudal uterine movement, $U(t)$, and abdominal acceleration magnitude, $|A(t)|$, for the subject who was asked to hold her breath during the measurement.

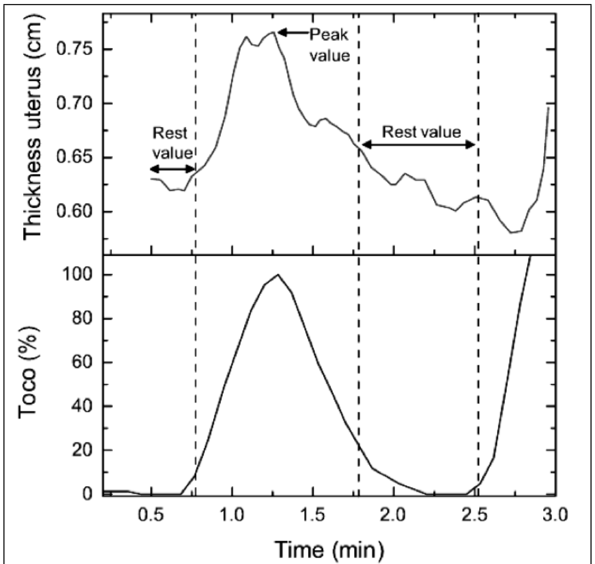

Fig. 2. Example of thickness increase during a contraction.

3) Contraction-induced uterine wall-thickness change: To determine the uterine wall thickness changes due to contractions, both the sagittal as well as transversal US recordings were analyzed. The analysis of the transversal US recordings was hampered by the cyclic cranial-caudal movements of the uterus resulting in out-of plane movements. To minimize the influence of these movements, US image sequences were triggered based on the signal from the accelerometer. The frame rate was therefore reduced from 25 Hz to about 0.3 Hz. This downsampling was allowed since the frequency at which thickness changes were observed was consistently lower than 0.15 Hz. Speckle tracking was used in the triggered image sequences to follow a region that showed high contrast between the uterine wall and the surrounding tissues. Within this region, the uterine wall thickness at the contraction peak, Δ_C, and during the resting period, i.e., between contractions, Δ_R, were derived and compared (see fig. 2). Contractions were defined as an increased abdominal strain detected by the tocodynamometer. The start (end) of a contraction was set at the time point where the increase (decrease) was 10% of the maximum value reached in the same contraction.

III. RESULTS

To derive uterine movement, $U(t)$, the average speckle size in the lateral direction was 0.10 ± 0.02 cm for both the uterus and the subcutaneous tissue. In the axial direction, a speckle size of 0.05 ± 0.01 cm and 0.03 ± 0.01 cm was found for the subcutaneous tissue and the uterus, respectively. Kernels of 0.3×0.8 cm were used. In fig. 1, the evolution of the cranial-caudal uterine movement, $U(t)$, derived by speckle tracking is compared to the magnitude of the abdominal acceleration, $|A(t)|$, for the additional patient who was asked to hold her breath during the periods 27-32 s and 76-81 s.

As can be seen also from fig. 1, both $U(t)$ and $|A(t)|$ have a sinusoidal pattern. The first two columns of table I report the amplitude, B, and frequency, f, of $U(t)$ for the other six patients. From the average values of B and f (6.8 ± 8.4 mm and 0.27 ± 0.07 Hz, respectively), we estimated an average peak velocity v of the uterine wall $v = 2\pi B f = 10.4 \pm 12.0$ mm/s.

Overall, correlation indicators $\rho = 0.51 \pm 0.09$ and $r = 0.85 \pm 0.06$ were found between $U(t)$ and $|A(t)|$, and their power spectra, respectively. The difference in peak frequency was 0 ± 0.03 Hz and not significant ($p > 0.05$).

TABLE I
UTERINE MOVEMENT PROPERTIES.

Case	B [mm]	f [Hz]	Δ_R[mm]	Δ_C [mm]	$\Delta_C - \Delta_R$ [mm]
1	0.5	0.37	5.0	7.2	2.2
2	0.3	0.21	6.8	7.9	1.1
3	24.9	0.23	3.9	4.9	1.0
4	6.3	0.19	-	-	-
5	3.5	0.31	2.8	2.3	-0.5
6	5.3	0.32	2.2	2.2	0.0

In fig. 2, an example of uterine wall thickness increase is shown and compared to the strain measured by the tocodynamometer. Uterine thickness could be reliably measured only in 5 of the 6 recorded cases because in one case the position of the placenta, anterior to the fetus, reduced the contrast between the uterus and the placenta. The results in the last 3 columns of table I report, for each analyzed case, the average values along 3 to 5 contractions.

IV. DISCUSSION

In an effort to improve the diagnostic value of the EHG, the mechanohysterogram was derived to characterize the mechanical activity of the pregnant uterus during contractions. The uterine wall was continuously observed by US and abdominal movements were measured by an accelerometer.

In all subjects a cyclic movement of the uterine wall was observed in the vertical direction (caudal-cranial). An additional dedicated measurement, in which this movement disappeared when the woman held her breath, confirmed that the underlying cause is respiration. This movement was not observed in the tissues between the uterus and the skin, probably because only the organs lying in the abdominal cavity within the peritoneum, like the uterus, are displaced by the diaphragm during respiration.

The amplitude of respiration-induced movements varied significantly among the subjects. Visual inspection of the US sequences confirmed that this variability is not due to outliers, but is indicative of subject-dependent characteristics. The modest correlation between $U(t)$ and $|A(t)|$, and the high correlation between their amplitude spectra and peak frequencies, clearly indicate that abdominal acceleration and uterine movement induced by respiration are correlated, but not in the time domain. We can 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 be ascribed to the complex mechanical transfer function between abdominal accelerations and uterine movements. The use of a system identification approach to process the signals prior to correlation analysis is under consideration for future research.

The detected uterine and abdominal movements due to respiration have implications for the interpretation and measurement of the EHG, because they imply movement of both the EHG signal source and of the measurement electrode. Since the EHG propagation properties have been recently suggested as the most promising indicators for preterm labor prediction [1], understanding the effect of uterine movement on the measured EHG propagation velocity would be particularly relevant. Quantifying the effect of uterine movement on EHG parameters was out of the specific scope of the study. Nevertheless, our results reveal an average peak velocity of the uterine wall movement (1.04 cm/s), much smaller than the values of EHG conduction velocity previously reported in the literature (4.9 - 53 cm/s) [1] [3] [4]. We expect therefore the effect of respiration-induced artifacts on the analysis of the EHG conduction velocity to be marginal. However, due to the yet unclear mechanism of EHG signal propagation, further research is needed.

During contractions, analysis of the mechanohysterogram revealed a change in thickness of the uterine wall. Wall thickness could not always be derived automatically as the contrast of the uterine wall in the US image depends on the placenta location, maternal obesity, and fetus position. In the majority of the analyzed cases, an increase in the uterine thickness was observed during contractions. Thinning of the uterine wall was observed during contractions in one patient. An increase in muscle thickness can be related to muscle shortening. Thinning can be explained based on the fact that, globally, the contraction of the uterus is isometric and that the tocodynamometer and the US probe measure uterine activity at different location. We can in fact hypothesize that, in some circumstances, a local thickening of the uterine wall is associated to a local thinning in a different location.

To the best of our knowledge, this is the first study that continuously observes the pregnant uterus during contractions by US. Previously, the pregnant uterine wall thickness was measured only intermittently during and between contractions [12]. The fact that no significant differences could be found in uterine thickness due to contractions might be due to the use of intermittent rather than continuous US recordings, and is in agreement with our hypothesis. However, only multiple simultaneous US recordings could confirm it.

V. CONCLUSIONS AND FUTURE WORK

In this study, for the first time, continuous US recordings are used to derive the mechanohysterogram and investigate the mechanical properties of the uterus during pregnancy and under the effect of contractions. Our methods, not intended as diagnostic tools, aim at improving EHG signal modeling and measurement. We highlighted two aspects that can be potentially determinant, namely, changes in uterine wall thickness during contractions and respiration-induced uterine wall movements. Our results suggest that these phenomena can play a role in the interpretation of EHG signal. Future work will focus on modeling and quantifying the effects of these phenomena on abdominal movements and on the EHG signal, possibly leading to improved EHG analysis.

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