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2008 Physiol. Meas. 29 829

(http://iopscience.iop.org/0967-3334/29/7/011)

IOP PUBLISHING PHYSIOLOGICAL MEASUREMENT
Physiol. Meas. **29** (2008) 829–841 doi:10.1088/0967-3334/29/7/011

Estimation of internal uterine pressure by joint amplitude and frequency analysis of electrohysterographic signals

Chiara Rabotti[1], Massimo Mischi[1], Judith O E H van Laar[2], Guid S Oei[2] and Jan W M Bergmans[1]

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

E-mail: C.Rabotti@tue.nl

Received 27 February 2008, accepted for pulication 12 May 2008
Published 26 June 2008
Online at stacks.iop.org/PM/29/829

Abstract
Monitoring the uterine contraction provides important prognostic information during pregnancy and parturition. The existing methods employed in clinical practice impose a compromise between reliability and invasiveness. A promising technique for uterine contraction monitoring is electrohysterography (EHG). The EHG signal measures the electrical activity which triggers the contraction of the uterine muscle. In this paper, a non-invasive method for intrauterine pressure (IUP) estimation by EHG signal analysis is proposed. The EHG signal is regarded as a non-stationary signal whose frequency and amplitude characteristics are related to the IUP. After acquisition in a multi-channel configuration, the EHG signal is therefore analyzed in the time–frequency domain. A first estimation of the IUP is then derived by calculation of the unnormalized first statistical moment of the frequency spectrum. The estimation accuracy is finally increased by identification of a second-order polynomial model. The proposed method is compared to root mean squared analysis and optimal linear filtering and validated by simultaneous measurement of the IUP on nine women during labor. The results suggest that the proposed EHG signal analysis provides an accurate estimate of the IUP.

Keywords: electrohysterography, medical signal processing, parameter estimation, time–frequency analysis, intrauterine pressure

1. Introduction

Premature birth is a major cause of long-term morbidity and it accounts for 69%–85% of neonatal deaths not caused by congenital malformations (Berkowitz and Papiernik 1993). An early prediction of preterm delivery by identification of the risk factors and accurate monitoring of the patients at risk is crucial for the treatment of preterm birth. In particular, an early diagnosis of delivery time can be achieved during pregnancy following the progression of the maternal uterine activity, i.e. frequency, duration and amplitude of the uterine contractions.

During labor, accurate monitoring of the uterine activity is essential to assess the condition of both mother and fetus. In particular, the fetal heart rate (FHR) is monitored in combination with the uterine activity in order to evaluate the fetal response to each contraction (Padhye *et al* 2004). After a uterine contraction, subtle changes of FHR or a total absence of FHR variability may in fact occur as first signs of fetal distress. Additionally, when complications occur, e.g. poor progress in labor, quantitative assessment of the uterine activity can guide the physician to opt for specific medical interventions, such as labor augmentation.

The contractile element of the uterus is the myometrium, which is composed of smooth muscle cells (Guyton and Hall 2006). The uterine contraction is the result of generation and propagation through the muscle cells of the electrical activity in the form of action potentials. Myometrial cells can generate action potentials or can be excited by action potentials generated by a neighboring cell. The transmission of electrical excitation is possible when cells are coupled by electronic synapses, which are referred to as gap junctions (Eswaran *et al* 2002). During pregnancy, poor coupling and low electrical conductance among the myometrial cells favor the maintenance of pregnancy; at term, gap junctions increase and form a low-resistance electrical path required for the occurrence of effective contractions (Garfield *et al* 1998).

The first result of a contraction is the internal uterine pressure (IUP) increase. Besides the traditional methods employing pelvic examination and symptomatic self-monitoring, the techniques used in clinical practice for uterine monitoring mainly rely on the direct (internal) or indirect (external) measurement of the IUP. External tocography is currently the most widely used technique to monitor the uterus during pregnancy and delivery (Garfield *et al* 1998). A tocodynamometer consists of a strain gauge transducer placed around the external surface of the abdomen and has the primary advantage of being non-invasive. However, deriving from an indirect mechanical measure of the pressure increase, the signal provided by external tocography is characterized by a low sensitivity, which can affect the estimation accuracy of contraction amplitude and duration (Eswaran *et al* 2002, Miles *et al* 2001).

During delivery, quantitative information concerning uterine functionality can be provided invasively, by measuring the amniotic IUP with an internal uterine pressure catheter (IUPC). However, the employment of an IUPC requires the rupture of the membranes and, due to the invasiveness of this device, it can increase the risk of infections and even cause damages to the fetus (Garfield *et al* 2002). Therefore, the IUPC is employed exclusively during parturition and its use is usually limited to complicated cases or during labor induction or augmentation.

An alternative method for monitoring the uterine activity is electrohysterography. The electrohysterogram (EHG) is the bioelectrical signal directly associated with the muscular activity of the myometrium. Generation and propagation of action potentials through an adequate number of cells are the primary causes of the uterine muscle contractions and of the consequent IUP increase. Therefore, the electrical activity recorded from the abdominal surface may provide essential information on the uterine activity and permit the prediction of the IUP associated with each contraction (Maul *et al* 2004).

The possibility of reliable and non-invasive assessment of the uterine activity has generated interest in the EHG analysis. In the literature, extensive research demonstrated the value of external EHG recordings in following the progress of the uterine contractility during pregnancy and parturition (Buhimschi and Garfield 1996). To this end, filtering techniques (Horoba *et al* 2001), the fast Fourier transform (Buhimschi *et al* 1997) and the wavelet transform (Eswaran *et al* 2002) have been employed for the EHG analysis; the results obtained were evaluated by visual comparison with the IUP or external tocography traces. However, only few studies focused on the EHG analysis as an alternative to the existing methods for a quantitative estimation of the uterine mechanical activity (Jezewski *et al* 2005, Skowronski *et al* 2006).

In Jezewski *et al* (2005), the contraction pattern estimated by the root mean square (RMS) value of the EHG was compared to the simultaneously recorded external tocogram. As the estimated contraction pattern was well correlated to the external tocographic signal, previous research could propose a reliable estimation of the contraction frequency, but a validation of amplitude and duration of the detected contractions was not possible. The use of optimal linear filtering for IUP prediction by the EHG signal analysis was recently investigated in Skowronski *et al* (2006). In this work, the simultaneously measured IUP was for the first time employed as a quantitative reference for the IUP predicted from the EHG analysis. According to this study, the IUP can be predicted from external EHG signals employing a Wiener filter on the rectified EHG.

In this paper, a new method for quantitative estimation of the uterine activity by the EHG analysis is proposed as a non-invasive alternative technique for IUP monitoring. We consider the EHG signal at each electrode as a non-stationary signal resulting from the summation of several frequency modulation (FM) processes (Duchêne *et al* 1995). The IUP increase is determined by the coexistence of two factors which in the myometrium, differently from skeletal muscles, are interrelated. These two factors, namely propagation of action potential, which is reflected in the spectral properties of the EHG signal, and amount of cells involved in the contraction, which is proportional to the amplitude of the EHG signal, are both taken into account to provide a first IUP estimate. A polynomial model of the relationship between the electrical and mechanical uterine activities is then used to improve the estimate quality. The measurement requires the sole employment of contact electrodes. Simultaneous IUP recordings by an IUPC were employed for a quantitative validation of the pressure estimates.

The proposed method was compared to the methods previously presented in the literature for quantitative estimation of the uterine mechanical activity. For the comparison, we employed an improved version of the RMS analysis-based method suggested by Jezewski *et al* (2005) and the optimal Wiener filtering proposed in Skowronski *et al* (2006).

2. Methodology

A schematic description of the proposed method for IUP estimation is shown in figure 1. The multichannel EHG signal and the invasively measured IUP were first recorded as described in section 2.1. The acquired signals were then preprocessed according to section 2.2; in particular, the EHG signal was made bipolar, down-sampled and analyzed in the time–frequency (TF) domain using the spectrogram. From the TF representation $\rho(t, f)$, the unnormalized first statistical moment $\Psi(t)$ was then calculated as the feature providing a first estimation of the contraction pattern. The energy of the EHG is concentrated in a limited frequency interval. Therefore, to optimize the signal-to-noise ratio (SNR), the first statistical moment was calculated in a limited bandwidth $[f_{\min}, f_{\max}]$, which was experimentally determined. A second-order polynomial model was then identified as described in section 2.4 to provide a better estimation of the IUP. The first- and second-order coefficients ($\widehat{b_i}$ and $\widehat{c_i}$) of the polynomial model were initially calculated for each single contraction by minimization of the mean squared error with the invasively measured IUP. Ultimately, for each channel the median

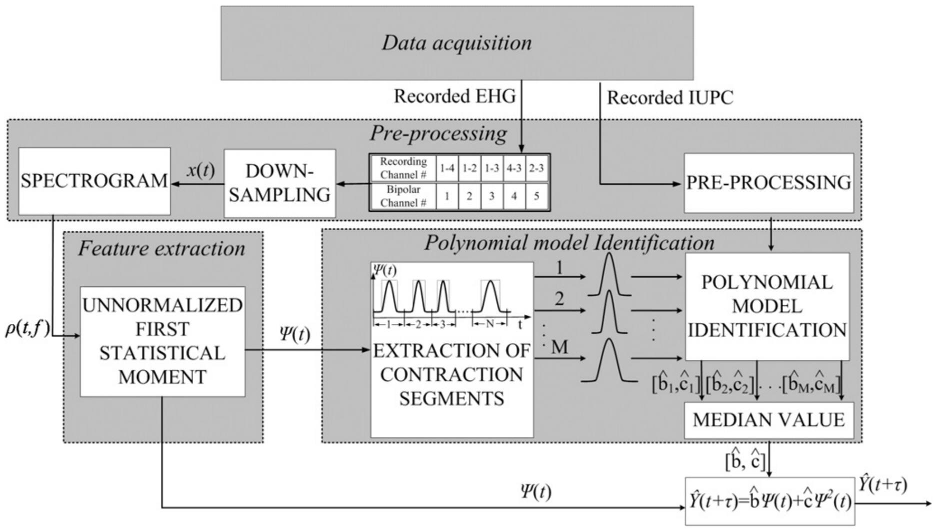


Figure 1. Scheme of the proposed methodology for data analysis for a single channel.

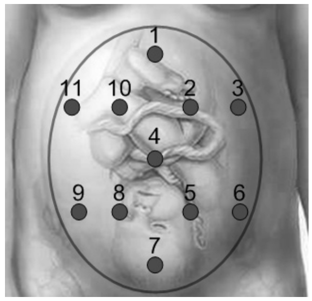
value of the coefficients over the available subjects was calculated. The model identified by the median values $\widehat{b}$ and $\widehat{c}$ of the coefficients was finally applied to the instantaneous mean frequency to provide the IUP estimate, $\hat{Y}(t)$.

2.1. Data acquisition

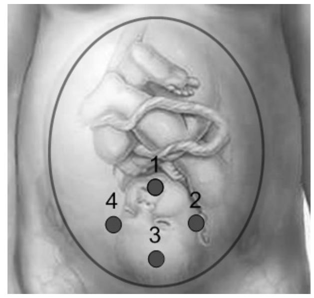
The experimental data were collected at the Máxima Medical Center in Veldhoven (The Netherlands). The study was approved by the ethical committee of the hospital. Nine women during labor underwent multichannel electrical EHG recordings after signing an informed consent. Six contact Ag–AgCl electrodes, consisting of four active electrodes, one ground electrode and one reference electrode, were placed on the subject's abdomen after skin preparation with an abrasive paste for skin impedance reduction. The IUP was simultaneously measured by an IUPC inserted in the uterine cavity due to a medical prescription. The total length of data recorded from each subject ranged from 22 to 90 min.

In order to identify a suitable electrode configuration, two 15 min measurements in labor were preliminarily performed with a higher number of active electrodes (11 instead of 4) placed on the abdomen as shown in figure 2(a), and a measure of the average SNR in each electrode was considered. During a contraction, the skeletal muscle EMG can be regarded as the major noise contribution. Considering the higher frequency band of skeletal EMG energy (Buhimschi *et al* 1997), the SNR was therefore calculated as the ratio of the signal in the frequency band between 0.1 and 5 Hz to that between 5 and 200 Hz during active contractions. In this preliminary study, the highest average SNR was experienced on the lower vertical median line of the abdomen, in particular on the region immediately below the umbilicus. These results have a twofold physiological explanation. On the one hand, in the vertical median line of the abdomen, the distance between the recording site on the skin and the signal source in the myometrium is reduced with respect to the lateral sides (Marque *et al* 2007). On the other hand, in the region surrounding the umbilicus the position of the uterus relative to the abdominal wall is constant even during contractions (Devedeux *et al* 1993), resulting in a better SNR.

How many electrodes are included in Monica?
3?



(a)



(b)

Figure 2. (a) Preliminary electrode configuration. (b) Final electrode configuration.

Based on the results of this preliminary analysis, the recordings employed in the present study were measured by four unipolar contact Ag–AgCl electrodes placed on the abdomen as shown in figure 2(b). The common reference for the electrodes was placed on the right hip. In order to obtain an efficient rejection of electromagnetic interference, a driven-right-leg electrode was placed below the reference electrode and the cables were actively shielded (van Rijn *et al* 1990). The position of the right leg electrode was chosen close to the reference rather than on the limb in order to avoid voltage oscillation due to the induced current flux through the body (van Rijn *et al* 1990).

A Koala M1333A (Philips Medical Systems, Best, The Netherlands) IUPC was inserted in the uterine cavity to measure the IUP.

The IUP and the EHG were simultaneously recorded and digitized at 20-bit resolution with an M-PAQ amplifier (Maastricht Instruments Ltd, The Netherlands), a 16-channel system for physiological measurements with programmable gain and sampling frequency. A sampling frequency of 1000 Hz was chosen in order to also allow the employment of the recorded signals by other applications, e.g. fetal ECG detection. For the power-line interference removal, the analog notch filter of the amplifier was employed.

2.2. *Preprocessing*

The unipolar EHG signal recorded at each active electrode was first made bipolar by subtracting the signals recorded at contiguous electrodes on the abdomen (figure 1). The employment of bipolar electrical signals has been demonstrated to effectively reduce a large portion of the noise affecting the EHG, e.g. the maternal electrocardiogram, part of the movement artifacts and the electromagnetic noise (Graczyk *et al* 1995).

The EHG and the IUP signals, recorded at 1000 Hz, were then down-sampled to 10 Hz, after low-pass anti-aliasing filtering at 5 Hz. The decrease of the sampling frequency, which reduces the computational time, is made possible by the low-frequency characteristic of the EHG (Devedeux *et al* 1993, Carré *et al* 1998, Marque *et al* 1986, Buhimschi *et al* 1997, Leman *et al* 1999).

For easy synchronization with the preprocessed EHG, the IUP signal was similarly down-sampled to 10 Hz. Additionally, in order to minimize spikes caused by movement artifacts, we employed a non-causal centered median filter of length $\pm$ 5 s to remove noise while retaining the IUP peaks (Skowronski *et al* 2006).

As the EHG is a non-stationary signal (Leman *et al* 1999), the employment of a time–frequency distribution (TFD) is a suitable frequency analysis approach. Since we are interested in the electrical energy, which is a quadratic signal, the class of quadratic TFDs was used (Andrieux *et al* 1987). In particular, in this study four different quadratic TFDs were tested, namely the Wigner–Ville distribution, the smoothed Wigner–Ville distribution, the Choi–Williams distribution and, finally, the spectrogram, which is obtained by the squared magnitude of the short-time Fourier transform of the signal $x(t)$ through a limited time window $w(\tau)$

$$\rho(t, f) = \left| \int_{-\infty}^{+\infty} x(\tau) w^*(\tau - t)\, \mathrm{e}^{-\mathrm{j}2\pi f \tau}\, \mathrm{d}\tau \right|^2, \tag{1}$$

where $(\cdot)^*$ is the conjugate operator.

The wavelet transform (WT) can also be employed for the analysis of non-stationary signals (Daubechies 1999) and its main advantage over other TFDs, such as the spectrogram, is the capability of performing a multi-resolution analysis in the TF domain (Rioul and Flandrin 1992). Although the WT is a time-scale representation in the first place, it is also suitable, in fact, for TF interpretation (Flandrin 1999) by formally relating the scaling parameter to the center frequency of the employed mother wavelet (Rioul and Vetterli 1991). Since we are interested in the analysis of the EHG signal energy distribution, the squared modulus of the WT, namely the scalogram, was calculated. The adopted mother wavelet was the Morlet wavelet, the most commonly used for TF analysis (Torrence and Compo 1998).

The most suitable values for the TFDs and the best TF distribution for EHG analysis were singled out by an iterative procedure aiming at the maximization of the average correlation coefficient r between the IUP estimated by the proposed method (before polynomial modeling, see section 2.4) and the IUP measured by the pressure transducer.

According to our experiments, the use of the spectrogram with a 70 s time window $w(\tau)$ resulted in the best estimation of the IUP. Moreover, with the prospect of on-line applications, the implementation of the spectrogram as the squared magnitude of the short-time Fourier transform results in a lower computational complexity with respect to other TFDs.

2.3. Feature extraction

The tension generated by the contracting myometrium and the consequent IUP increase are dependent on the speed of action potentials from cell to cell and on the amount of muscle cells involved in the contraction (Garfield *et al* 1998); in smooth muscles, these two phenomena are mutually dependent, as propagation requires recruitment of multiple cells. The excitation rate of smooth muscle cells, which is the counterpart of the firing rate for skeletal muscle EMG, is an additional factor which contributes to the IUP increase. All these factors are reflected in the frequency spectrum of the EHG signal, which can be therefore regarded as the result of a FM process. Additionally, the EHG signal at each electrode is the signal generated by the muscular contraction on a macroscopic scale, i.e. a signal originating from the combined contributions of the individual muscle cells activated underneath the electrode. Consequently, the EHG at each electrode is regarded as the result of a FM multi-component signal where the IUP is related to the modulating signal (Duchêne *et al* 1995). A first estimate of the contraction pattern can hence be provided by the average frequency. The average frequency $f_1(t)$ of a signal, represented in the TF domain by the spectrogram $\rho(t, f)$ as in (1), can be expressed as

$$f_1(t) = \frac{\int_0^\infty f \rho(t, f)\, \mathrm{d}f}{\int_0^\infty \rho(t, f)\, \mathrm{d}f}, \tag{2}$$

which also corresponds to the first statistical moment with respect to the frequency (Boashas 2003). The use of (2) is common for spectral analysis of the skeletal muscle EMG signals and for assessment of fiber conduction velocity (Sörnmo and Laguna 2005). However, differently from skeletal muscles, the force generated by the uterus is related to both the propagation properties of the action potentials, which are reflected in the spectral characteristic of the EHG signal, and the amount of cells involved in the contraction, which is proportional to the amplitude of the EHG signal. A measure of the signal amplitude is provided by its energy (Proakis and Manolakis 1996)

$$E_x(t) = \int_0^{\infty} \rho(t, f)\,\mathrm{d}f. \tag{3}$$

The IUP increase is the consequence of the well-coordinated contraction of a substantial number of cells. Therefore, the simultaneous increase of both the frequency-related and amplitude-related features of the EHG signal determines the establishment of the IUP wave. By multiplying (3) and (2), a first estimation of the IUP can be therefore derived, which corresponds to the unnormalized first statistical moment $\Psi(t)$ of the TF representation $\rho_z(t, f)$ in a selected frequency band $[f_{\min}, f_{\max}]$

$$\Psi(t) = \int_{f_{\min}}^{f_{\max}} f\rho(t, f)\,\mathrm{d}f. \tag{4}$$

Based on our measurements and in agreement with other studies (Buhimschi *et al* 1997, Leman *et al* 1999, Maner *et al* 2003, Marque *et al* 1986), the most suitable integration interval $[f_{\min}, f_{\max}]$ for IUP estimation resulted in the frequency band [0.3 Hz, 0.8 Hz].

2.4. Polynomial model identification

The first unnormalized statistical moment calculated from the TF representation can be further processed in order to increase the accuracy of the estimate. To this end, we adopted a polynomial model for taking into account the offset, gain and nonlinear effects describing the relationship between the electrical and the mechanical activities of the uterus.

Two different factors can be accounted for nonlinearities: the physiology underlying the contraction of the myometrium and the possible consequences of muscle fatigue. The first factor can be explained considering that each electrode records the electrical activity localized below or in the neighborhood of the electrode position. Nevertheless, the IUP increase is the result of the simultaneous contraction of an adequate number of cells, and it is associated with a widespread electrical activity of the whole myometrium. Therefore, localized or unsynchronized electrical activities can be recorded by the neighboring electrodes without being necessarily followed by a linearly related IUP increase. The second factor which can cause a nonlinear relation between mechanical and electrical uterine activities is muscle fatigue, which may inhibit a proper mechanical reaction of the myometrium to the electrical activation.

A second-order polynomial model resulted as a suitable representation of the relationship between the unnormalized first statistical moment of the EHG signal TF representation and the simultaneously measured IUP. The use of higher order polynomial models was also investigated, but no improvement was experienced.

Furthermore, as the tension generated by the myometrium is the result of the action potential spreading in the muscle tissue, the IUP increase is always temporally delayed with respect to the electrical activation. Therefore, the delay τ_k between the IUP recorded by the catheter and the first unnormalized moment calculated in each channel k was also included in the model.

We indicate by $\underline{\Psi_k} = (\psi(t_1), \psi(t_2), \ldots, \psi(t_N))$ the digitized instantaneous mean frequency calculated in each channel k. The delayed IUP estimate $\underline{\widehat{Y}_k} = (y(t_1 + \hat{\tau}_k), y(t_2+\hat{\tau}_k), \ldots, y(t_N+\hat{\tau}_k))$ is therefore derived by a polynomial expansion of $\underline{\Psi_k}$ with coefficients $\widehat{a_k}$, $\widehat{b_k}$ and $\widehat{c_k} \in R$

$$\underline{\widehat{Y}_k} = \widehat{a_k} + \widehat{b_k}\underline{\Psi_k} + \widehat{c_k}\underline{\Psi_k^2}. \qquad (5)$$

In (5), $\widehat{a_k}$ models the offset, $\widehat{b_k}$ the gain and $\widehat{c_k}$ the second-order nonlinearities of the relationship between the first unnormalized moment calculated in each channel k and the IUP. The pressure in the uterus in the absence of active uterine contractions is usually referred to as baseline tone (Steer 2004). Since the measured IUP baseline tone is affected by factors that are not related to the uterine activity (Steer 2004), the baseline tone was detected by the method described in Jezewski *et al* (2005) and digitally removed on the basis of the first 2 min of recording. As the same procedure was applied to $\underline{\Psi}$ prior to identification of the model coefficients, the constant term $\widehat{a_k}$ in (5) was set to zero. The values of $\widehat{b_k}$ and $\widehat{c_k}$ were then estimated by a least squares method where the invasively recorded IUP, $\underline{Y} = (y(t_1), y(t_2), \ldots, y(t_N))$, was regarded as the reference signal. Indicated by N the number of samples, the squared error $\underline{\epsilon_k}$ to be minimized is expressed as

$$\underline{\epsilon_k} = \frac{1}{N}\|\underline{Y} - \underline{\widehat{Y}}_k\|^2. \qquad (6)$$

By defining the matrix

$$\mathbf{X}_k = \begin{bmatrix} \psi_k(t_1) & \psi_k^2(t_1) \\ \psi_k(t_2) & \psi_k^2(t_2) \\ \vdots & \vdots \\ \psi_k(t_N) & \psi_k^2(t_N) \end{bmatrix},$$

and the parameter vector $\underline{\hat{P}_k} = [\hat{b_k} \quad \hat{c_k}]$, the least squares solution (Manolakis *et al* 2005) is given by

$$\underline{\hat{P}_k} = \left(\mathbf{X}_k^t\mathbf{X}_k\right)^{-1}\mathbf{X}_k^t\underline{Y}. \qquad (7)$$

The values of $\widehat{b_k}$ and $\widehat{c_k}$ were first estimated separately in contiguous contraction segments of variable length N for each patient and channel. After an automatic contraction detection by the method described in Jezewski *et al* (2005), each contraction segment included one contraction and part of the baseline tone preceding and following the contraction itself. Indicated by M the total number of detected contraction segments for each channel, the definite values of the model coefficients $\widehat{b_k}$ and $\widehat{c_k}$ were finally calculated as the median value of the coefficients $\widehat{b_{k_i}}$ and $\widehat{c_{k_i}} (i = 1, \ldots, M)$ obtained in the contraction segments from all the subjects. The median value rather than the average value was chosen to ensure robustness with respect to possible outliers.

The delay between the unnormalized first moment and the IUP signals was initially calculated by maximization of their cross-correlation function for each recording. For each channel k, the average delay τ_k across all the subjects was then considered for the entire dataset.

3. Results

Previous studies for estimating the uterine mechanical activity by EHG processing mainly comprised the calculation of the RMS value of the EHG signal and, more recently, the

Table 1. Average results.

Method	r ($p < 0.01$)	RMSE (mmHg)
Optimal linear filtering	0.5 ± 0.16	11.4 ± 3.12
RMS	0.36 ± 0.16	13.17 ± 4.62
Proposed method	0.73 ± 0.11	13.47 ± 6.67

employment of optimal linear filtering (Horoba *et al* 1999, Skowronski *et al* 2006). These two algorithms were tested on each channel of our dataset to assess the proposed method. The comparison aimed at the evaluation of the methods in the prospective of non-invasive measurements in a clinical setting.

According to the method proposed by Horoba *et al* (1999, 2001), for each bipolar down-sampled signal we calculated the RMS values in 60 s sliding Hamming windows. Then, prior to comparison with the results obtained by the other methods, the model defined in (5) was applied to the calculated RMS series according to the procedure previously described.

For the implementation of the Wiener filter (Skowronski *et al* 2006), further preprocessing was needed to normalize, down-sample and rectify the preprocessed signal $x(t)$. The performance of the algorithm described in Skowronski *et al* (2006) was further improved by removing the mean value from both the rectified EHG signal and the IUPC signal prior to training the filter coefficient. For each channel and patient, a set of weights was then calculated on the basis of the entire recording employing linear regression. For each channel, a set of weights was then obtained by averaging the values across the examined subjects. The final results were eventually derived by filtering the rectified EHG signals from all the subjects employing the calculated average weights.

The results obtained by the proposed method for IUP estimation were compared to those provided by optimal filtering and RMS analysis in terms of the correlation coefficient r and root mean squared error (RMSE) between the IUP estimate and the IUP measured by the catheter. The correlation coefficient r and the RMSE are important figures of merit for the characterization of the estimate. As the correlation coefficient is a measure of similarity in shape between two waveforms, a high value of r between the real IUP and its estimate can be directly related to a high probability of detecting the correct number of contractions. The RMSE, on the other hand, is influenced by scaling factors and dc offset. Therefore, for a fair comparison with optimal linear filtering, the RMSE of the estimate provided by RMS analysis and by the proposed method was calculated after removal of the average value from both the IUPC signal and the estimate. Note that the RMSE retains the same units of pressure of the desired signal (mmHg).

The results provided by the proposed method, RMS analysis and optimal linear filtering are shown in table 1, where the average values of r and RMSE across all channels and patients are reported together with their inter-patient variability. Optimal linear filtering provides the best average results in terms of RMSE (11.38), while the highest correlation coefficient is achieved by the proposed method ($r = 0.73$).

In figures 3–5, an example of IUPC recording and corresponding IUP estimate is presented for each of the three methods for the same channel of the same subject.

By employment of the polynomial model, the estimated accuracy improved for both the RMS analysis and the unnormalized first statistical moment. Especially for the proposed method, the average correlation coefficient with the invasively recorded IUP improved from $r = 0.59$ to $r = 0.73$; the root mean squared error improved from RMSE = 17.20 mmHg to RMSE = 13.47 mmHg.

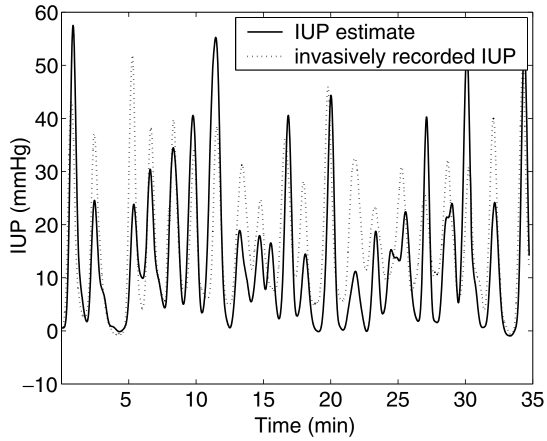


Figure 3. Example of the IUP estimated by the proposed method for patient 8, bipolar channel 3. For the entire waveform, $r = 0.70$ and RMSE = 9.67 mmHg.

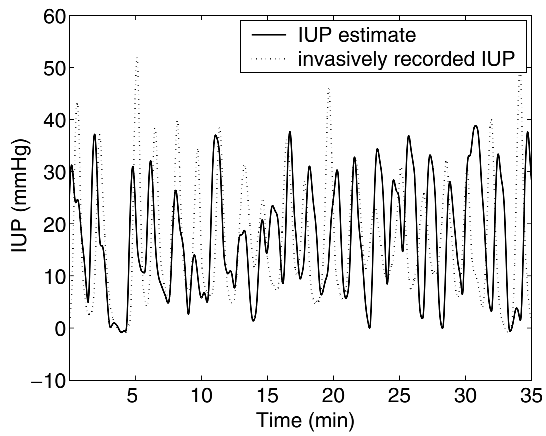


Figure 4. Example of the IUP estimated by the RMS analysis method for patient 8, bipolar channel 3. For the entire waveform, $r = 0.50$ and RMSE = 9.5 mmHg.

Table 2. Model parameters.

Channel	b	c	$\tau(s)$
1	2.8358	−0.008 2974	10
2	3.5073	−0.1057	8.3
3	8.1703	−0.061 961	10.7
4	3.3777	−0.008 3798	11.2
5	6.8159	−0.092 923	9.6

Table 2 shows the final values of the model coefficients $\widehat{b_k}$ and $\widehat{c_k}$ employed for the proposed method reported together with the average time delay τ_k for each channel.

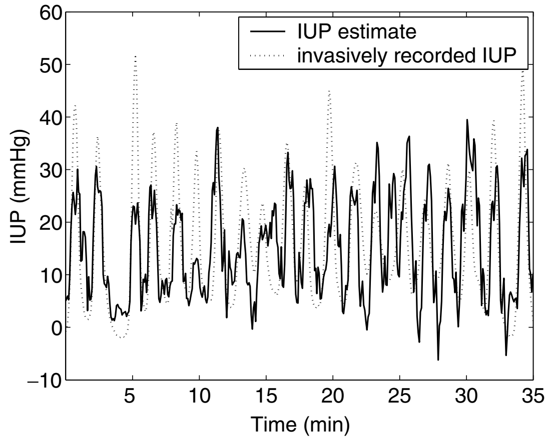


Figure 5. The IUP estimated by optimal linear filtering for patient 8, bipolar channel 3. For the entire waveform, $r = 0.60$ and RMSE $= 9.78$ mmHg. The removed mean value was restored for both waveforms on the basis of the mean value of the invasively recorded IUPC.

4. Discussion and conclusions

In this paper we propose a non-invasive method to estimate the IUP that is based on the joint analysis of amplitude and time–frequency features of the EHG signal. The method was tested on a set of measurements from nine women during delivery. The results were compared to those provided by the other two methods proposed in the literature for a quantitative estimation of the uterine mechanical activity, namely the optimal linear filtering and an improved version of the RMS analysis. The comparison aimed at the evaluation of the methods in the perspective of non-invasive measurements. By simultaneously recording a four-channel EHG signal and the IUPC output, we could reliably assess the IUP estimates provided by the methods.

In terms of the correlation coefficient with the invasively recoded IUP, the proposed method resulted in a significantly increased correlation with respect to the RMS analysis and the optimal linear filtering. When the root mean squared error between the estimated IUP and the invasively recorded IUP is considered, the three methods resulted in RMSE values of approximately the same order of magnitude, with the optimal linear filtering approach slightly outperforming the RMS analysis and the proposed method.

With reference to the methodology, the RMS analysis has the great advantage of being simple and suitable for real-time applications. The optimal linear filtering suggests a technical approach aimed at the identification of a linear transfer function between the rectified EHG signal and the IUP. The physiological assumptions of these two methods can be summarized in the use of the EHG amplitude, either in terms of the EHG signal envelop or in terms of the rectified EHG signal, as indicative of the tension produced by the contracting myometrium. On the other hand, the proposed method was fundamentally conceived on the basis of physiologic phenomena underling the generation of the recorded signals and their relationship.

The aim of this study is the non-invasive estimation of the IUP by EHG signal processing. In this context, the obtained good correlation coefficient with the invasively recorded IUP suggests that the proposed physiology-based approach should be further pursued. However, for the proposed method, as well as for the other investigated methods, the amplitude difference between the invasively recorded IUPC and the provided estimate was often larger than

10 mmHg, which corresponds to the IUPC signal accuracy reported in the literature (Dowdle 2003, Arulkumaran *et al* 1991). In the future, we will therefore focus on the improvement of the proposed methods for IUP estimation. In particular, considering the results of the present study as evidence for the nonlinear relationship between the extracted feature and the invasively recorded IUP, future work will explore the estimation accuracy by other nonlinear models which are possibly more suitable for characterization of the underlying physiological processes. The good results of the estimate suggest that the coefficients of the polynomial model did not show significant variations across the considered subjects. However, in the perspective of introducing the proposed method in everyday clinical practice, the proposed approach could support dedicated studies aimed at the identification of more complex models, possibly including additional parameters for the general characterization of patient differences.

In general, the proposed method, due to the adopted physiology-based approach, may offer additional insight for a better understanding of the uterine muscle activity. As the EHG signal is associated with the primary cause of the uterine contraction, we believe that the EHG signal analysis has great potentiality beyond the estimation or prediction of the uterine mechanical activity. Nevertheless, many aspects related to the uterine muscle contraction process still need to be clarified. Future research will therefore include the propagation properties of the EHG signal with the ultimate goal of providing a reliable and non-invasive technique for preterm labor prediction.

Acknowledgment

This work was supported by the Dutch Technology Foundation STW.

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