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Characterization of Uterine Peristaltic Waves by Ultrasound Strain Analysis

Yizhou Huang, *Graduate Student Member, IEEE*, Connie Rees, Federica Sammali, Celine Blank, Dick Schoot, and Massimo Mischi, *Senior Member, IEEE*

***Abstract*—Uterine peristalsis (UP) is a wavelike uterine motion that plays an important role in the generation of intrauterine streams for menstrual emptying and to support embryo implantation. Our understanding of uterine mechanical behavior is hampered by a lack of quantitative analysis. Here, we propose a spatiotemporal analysis of UP by ultrasound speckle tracking and dedicated strain analysis. We aim at characterizing UP propagating around the endometrial cavity through the anterior and posterior walls of the uterus. To this end, velocity and coordination features are proposed in this study. We investigated a total of 11 healthy volunteers during their natural menstrual cycle and 81 patients undergoing *in vitro* fertilization (IVF) treatment. They all received multiple 4-min 2-D transvaginal ultrasound scans. Significant differences in propagation velocity were found among different phases of the menstrual cycle, which are in line with the expected uterine behavior. A significant difference in coordination was found between the group of women with successful (pregnancy at 11 weeks) and unsuccessful IVF. This result suggests that the ability to generate coordinated UP represents an important factor for IVF success. The proposed UP quantification may represent a valuable clinical tool for improved understanding of UP and improved decision-making in the context of IVF procedures.**

***Index Terms*—*In-vitro* fertilization (IVF), quantitative ultrasound, speckle tracking, uterine peristalsis (UP), uterine strain.**

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This work involved human subjects or animals in its research. Approval of all ethical and experimental procedures and protocols was granted by the Relevant Medical Ethical Committee of Catharina Hospital Eindhoven (The Netherlands) under Approval No. NL52466.10.15, ClincalTrails.gov under Approval No. NCT02310802, and Ghent University Hospital (Belgium) under Approval No. B670201629814.

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I. Introduction

WORLDWIDE, approximately one in six couples experiences infertility during their reproductive ages (from 20 to 44 years old) [1]. Most women with (sub)fertility problems seek clinical support from assisted reproductive technologies, such as *in vitro* fertilization (IVF). In the last decade, the number of IVF cycles performed every year has increased by over 20% [2], [3]. However, the success rate of IVF treatment remains below 30%, with only a 4% increase [2], [3]. An IVF cycle consists of the preparation of the patient with exogenous hormones, after which the developed oocytes (eggs) are retrieved from the ovarian follicles and fertilized *in vitro*. The resulting embryos are then transferred back into the uterine cavity. Subsequent successful implantation of the embryo in the uterine wall leads to pregnancy. Several studies indicate that dysfunction of uterine contractility is one of the possible reasons hampering successful embryo implantation [4]–[7].

The uterine body consists of three parts: an outer serosal layer, an inner lining called endometrium, and an intermediate muscle layer called the myometrium (see Fig. 1). Uterine contraction of a nonpregnant uterus, which refers to the shortening of the uterine muscle, was first mentioned in 1937 by Dickinson based on bimanual palpation [8]. Uterine contraction is reported to mostly occur around the endometrium, acting as a wave propagating alongside the endometrium. The resulting rhythmic uterine deformation (motion) is also known as uterine peristalsis (UP) [7]. Due to the influence of hormone levels, the UP patterns change in terms of direction, frequency, velocity, and amplitude during different phases of the menstrual cycle. In particular, during the luteal phase, when opposing contraction waves are often generated to keep the embryos inside the endometrial cavity and facilitate their implantation. Women suffering from infertility problems are also likely to suffer from uterine disorders, such as endometriosis and adenomyosis, or endocrine disbalances, which can affect UP and hamper embryo implantation. Therefore, a reliable assessment of the uterine activity outside pregnancy can be expected to provide valuable insight into the influence of UP on IVF failure.

Currently, most studies on the assessment and characterization of UP are based on qualitative measurements by visual inspection of transvaginal ultrasound (TVUS) recordings [7], [9]–[11], [12]. Visual characterization of the uterine activity

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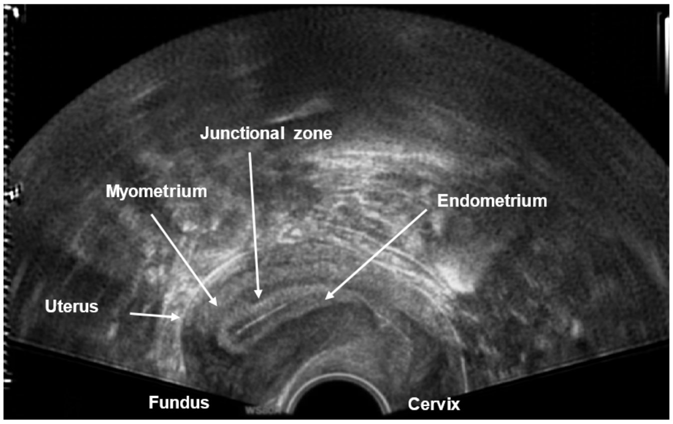

Fig. 1. Example of acquired ultrasound (US) frame from an *in vivo* recording during the late follicular (LF) phase.

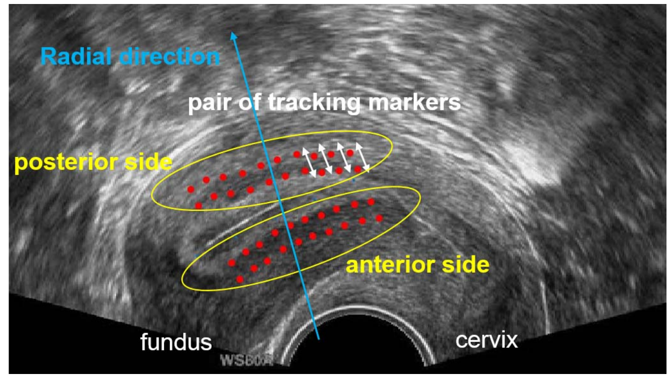

Fig. 2. Tracking marker grid (red dots) positioning along the anterior and posterior walls of the endometrium. TVUS recording acquired from a healthy volunteer during the LF phase.

in this manner is rather challenging and subjective, especially during the late luteal (LL) phase of the menstrual cycle, or right before embryo transfer (ET) during IVF treatment, when the uterus is expected to be more quiet compared to the other phases. A recent study shows that three medical professionals share only mild agreement on the direction and timing of UP by visual inspection of 80 TVUS recordings [13]. The lack of an objective and quantitative analysis of uterine contractility thus limits the ability to characterize UP and improve the success of IVF treatment. Following up on our recent work on dedicated ultrasound (US) speckle tracking for quantitative analysis of uterine motion [14], this article presents a quantitative assessment of the uterine activity focusing on the propagation of UP during a natural menstrual cycle as well as during an IVF cycle. In particular, velocity, direction, and coordination of UP are assessed.

To quantify UP, uterine motion throughout the US recording must first be assessed. In the field of US-based speckle tracking, there are two major approaches to estimate motion, namely, block matching (BM) and optical flow (OF). BM segments the image into blocks and seeks the best matches of these blocks in subsequent frames based on a chosen matching criterion. On the other hand, OF is a pixel-to-pixel gradient approach that estimates the velocity of the target object between two subsequent frames. In our study, OF is chosen over BM due to its higher sensitivity to subpixel motion [15]. Moreover, as introduced by Bouguet [16], the tracking accuracy of OF can be further improved by implementing iterative spatial warping. The adopted OF method was first optimized and validated *in vitro* using a dedicated setup with human *ex vivo* uteri [17].

For each TVUS recording, tracking markers (TMs) were manually placed along both the anterior and posterior walls of the endometrium (see Fig. 2). The TMs were always positioned starting 5 mm from the fundal extremity of the endometrium and moving toward the cervix, spaced 2.5 mm from each other. Movements of these TMs were tracked over time. Radial strain rates (RSRs) were derived between each pair of TMs to generate a time–space representation of UP along the endometrium. Relevant features, such as UP velocity, direction, and coordination, were then extracted from the resulting time–space representation.

In vivo validation was carried out to test the feasibility of our proposed method. Healthy volunteers underwent four TVUS scans acquired during four selected phases of the natural menstrual cycle, namely, during menstruation (Menses), LF, early luteal (EL), and LL phases. The proposed method was evaluated for its ability to distinguish the peristaltic patterns among the selected phases.

The method was also evaluated in the context of IVF. TVUS recordings were performed on 81 patients during an IVF treatment cycle. Our validation aimed at testing the ability of the proposed UP features to predict the successful and unsuccessful pregnancy groups before ET into the uterine cavity.

II. Methodology

A. Data Acquisition

In this study, US acquisitions on 11 healthy volunteers (age: 31.2 ± 5.2 years; body mass index (BMI): 22.6 ± 2.3 kg/m^2) were performed at the Catharina Hospital Eindhoven (Eindhoven, The Netherlands) [18]. These healthy volunteers underwent two subsequent 4-min TVUS B-mode scans using a Samsung-Medison WS80A scanner equipped with a V5-9 transvaginal probe during Menses, LF, EL, and LL phases.

In addition, US acquisitions in women undergoing IVF were collected from two studies. From the IMPLANT 1 study [19], aiming at testing inhibitors of the uterine activity, US recordings in 65 control patients (age: 31.4 ± 3.1 years; BMI: 23.4 ± 4.1 kg/m^2) receiving placebo were collected. These patients underwent fresh day-3 ET with one or two embryos, one of which being of good quality according to the Istanbul conference Alpha criteria [20]. They had history of no more than one failed IVF cycle and used a gonadotropin-releasing hormone (GnRH) antagonist protocol with a single injection of human chorionic gonadotropin (HCG) for triggering ovulation. Being part of the control (placebo) group, the uterine activity was influenced by injected hormones only. For all patients, 4-min B-mode TVUS recordings were acquired 4 h before ET. Being a multicenter study, various brands of ultrasound

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scanners and probes were used. More details on the patient enrolment and IVF protocol can be found in [19].

At Ghent University Hospital, 4-min B-mode TVUS recordings were acquired 1 h before ET in 16 patients (age: 32.1 ± 4.7 years; BMI: 25.9 ± 4.7 kg/m^2) undergoing day 5 ET with the single ET based on the Istanbul conference definition [20]. The enrolled patients received GnRH for follicle stimulation and HCG injection 34–36 h before oocytes retrieval. The 4-min B-mode TVUS recordings were acquired 1 h before ET using Samsung-Medison WS80A scanner equipped with a V5-9 transvaginal probe. More details can be found in [21].

The IMPLANT 1 study was retrospective, while the Catharina Hospital and Ghent University Hospital studies were prospective, with the sonographers being properly instructed on the imaging requirements for this study.

The acquisition frame rate ranged from 25 to 30 frames/s. All the recordings were converted to audio video interleave (AVI) format for further analysis.

Due to motion artifacts during insertion and positioning of the probe in the uterine cavity as well as during its removal, the time length for all 2-D recordings was shortened to 3 min by cropping a certain part of the recording in the beginning and at the end.

B. Ultrasound Speckle Tracking

US speckle is caused by the interference of the backscatter US waves received by the transducer. Tissue forms a unique speckle pattern that can be tracked over time. Therefore, tissue motion can be assessed by tracking the movement of the speckle pattern. The highest endometrial wave velocity is less than 2 mm/s [10]. Therefore, with an acquisition frame rate and pixel size equal to 30 Hz and 0.065 mm, respectively, uterine motion between subsequent frames was smaller than one pixel. To deal with such subpixel motion and provide accurate tracking results, OF was employed to perform speckle tracking in this study. With I being the intensity of a certain pixel, the pixel velocities in the x- and y-directions, υ_x and υ_y, are thus represented by the intensity gradients in the spatial (x, y) and temporal (t) domains according to

$$\upsilon_x \frac{\partial I}{\partial x} + \upsilon_y \frac{\partial I}{\partial y} + \frac{\partial I}{\partial t} = 0. \tag{1}$$

To solve the above ill-conditioned equation, Lukas and Kanade [22] proposed to estimate the motion of a block instead of a pixel under the assumption of constant flow within the block. The velocities in both directions are then obtained by least square estimation. After that, the pixel location in the target frame is updated according to the estimated velocities.

The accuracy of OF can be further improved by applying an iterative refinement approach under the assumption of small motion [16]. In this study, OF was first applied to track the motion of a selected speckle pattern between the reference frame and the target frame. Based on an initial estimation $\underline{\upsilon}_1$, the target frame was warped by the 2-D interpolation. In this way, the movement of the speckle pattern was partly retrieved between the reference and the target frames. In the following second iteration, a new estimation of residual motion, $\underline{\upsilon}_2$, was derived between the reference and the warped target frames. This process was applied iteratively until the residual motion $\underline{\upsilon}_n$ converged to a very small value or it reached the maximum number of iterations M. The final estimation of the pixel motion, $\underline{\upsilon}_{\text{end}}$, was then calculated as the sum of the initial motion and all residual motions, $\underline{\upsilon}_{\text{end}} = \sum_{\text{iter}=1}^{M} \underline{\upsilon}_{\text{iter}}$.

Apart from applying this iterative refinement, the choice of the block size is also crucial for OF to obtain accurate tracking results. For small blocks, the tracking becomes sensitive to local motion and noise, while for large blocks, the hypothesis of constant flow may be violated. The optimization of the block size was carried out *ex vivo* using the dedicated experimental procedure proposed in [17]. The optimized block size resulted to be 41 × 41 pixels^2 (around 2.6 × 2.6 mm^2).

C. Anatomical Strain Framework

UP is often observed close to the endometrium, in the junctional zone, rather than in the myometrium [23]. TMs were therefore selected along both the anterior and posterior walls of the endometrial cavity at the first frame of each TVUS recording.

A semiautomatic approach was employed to maintain the same distance between each pair of neighboring TMs both in the radial and longitudinal directions (see Fig. 2). In this study, the distance was chosen corresponding to the optimal block size.

Out-of-plane (OOP) motion is a frequent phenomenon during *in vivo* 2-D TVUS acquisition. The occurrence of OOP motion is mainly caused by the movement of the imaged target in the 3-D perpendicular to the observation plane. Sometimes, it might also be caused by the influence of probe motion and patient movement. Once OOP motion occurs, the speckle pattern being tracked moves out of the observation plane. The resulting decorrelation of the speckle pattern will lead to speckle tracking errors. To mitigate the influence of OOP motion on the accuracy of 2-D speckle tracking with *in vivo* data, we proposed a two-step approach.

In the first step, the middle lining of the endometrium was manually drawn and ten TMs (TMs$_{\text{midline}}$) with isotropic distance were generated along the middle lining [see Fig. 3(a)]; speckle tracking was applied to the TMs$_{\text{midline}}$ through the entire recording. We estimated the global translation of the endometrium (x_n, y_n) for each frame n by averaging the movement of TMs$_{\text{midline}}$ in the horizontal and vertical directions. After that, we estimated the rotation of the endometrium (θ_n) by linear fitting based on the coordinates of TMs$_{\text{midline}}$ [see Fig. 3(b)]. In this way, even if part of the endometrium was affected by OOP motion, the global translation and rotation could still be recovered from the rest of TMs$_{\text{midline}}$, which were not affected by OOP motion.

Once the global translation (x_n, y_n) and rotation (θ_n) of the endometrium were obtained through the entire recording, the coordinates of the TMs were updated for each frame n as

$$\begin{bmatrix} X_n \\ Y_n \end{bmatrix} = \begin{bmatrix} \cos(\theta_n) & -\sin(\theta_n) \\ \sin(\theta_n) & \cos(\theta_n) \end{bmatrix} \times \begin{bmatrix} X_{n-1} \\ Y_{n-1} \end{bmatrix} + \begin{bmatrix} x_n \\ y_n \end{bmatrix}, \quad n = 2, \ldots, N \tag{2}$$

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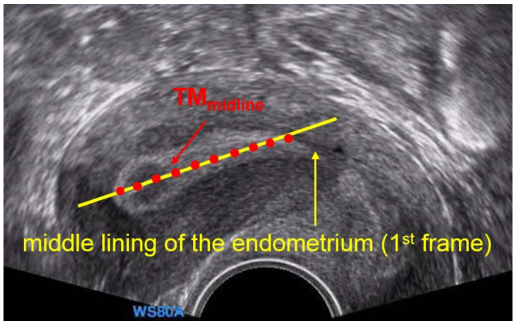
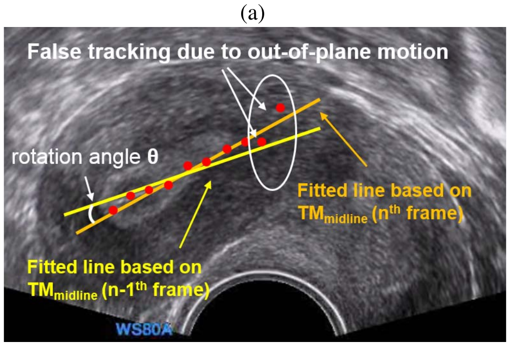


(a)



(b)

Fig. 3. (a) Ten $\text{TMs}_{\text{midline}}$ selected along the middle lining of the endometrium. (b) OOP motion started from the n_{th} frame. Although speckle tracking failed with two TMs (indicated with white arrow), the global rotation of the endometrium could still be recovered by the fit lines between the subsequent frames.

where N is the total number of frames and (X_1, Y_1) represents the coordinates of the TMs selected in the first frame, relative to the uterine anatomy.

A quantitative measure was introduced to evaluate the quality of the TVUS recordings. Pierson correlation coefficient (PCC) was here used to test the similarity of the speckle patterns between the subsequent frames [24]. The quality of the recording was then determined by the average PCC over all TMs. Recordings with an average PCC > 0.8, indicating negligible speckle decorrelation due to OOP motion in subsequent frames, were accepted for further analysis.

In the second step, speckle tracking was then applied to TMs. For example, to estimate motion between the $(n-1)$th and the nth frames, instead of updating the coordinates of TMs based on their displacements, the coordinates were updated to (X_n, Y_n), according to (2). As a result, speckle tracking is applied only between two subsequent frames. In this way, even if OOP motion caused decorrelation and poor tracking, the tracking error remains limited between two frames without further accumulation. With this approach, tracking is performed for TMs representing consistent anatomical regions, enabling further interpretation of the results as associated with the uterine anatomy and geometry.

The author was blinded to the acquisition characteristics, such as the success of IVF treatment and the menstrual phases when positioning the TMs.

D. Radial Strain Rate Analysis

Strain rate imaging is one of the most widely used approaches for measuring regional or global deformation of the muscle. Therefore, to characterize UP, RSR was derived from both the anterior and posterior walls of the endometrium.

RSR was calculated from the ratio between the variations in the distance between each pair of TMs in the radial direction (see Fig. 2) and their original distance, which is given as

$$\text{RSR}_n = \frac{\sqrt{(\upsilon_{x1}-\upsilon_{x2})^2+(\upsilon_{y1}-\upsilon_{y2})^2}}{D_{n-1}}, \quad n = 2, \ldots, N \quad (3)$$

where $(\upsilon_{x1}, \upsilon_{y1})$ and $(\upsilon_{x2}, \upsilon_{y2})$ represent the estimated velocities in the x- and y-directions from the chosen pair of TMs between the $(n-1)$th and the nth frames, D_{n-1} represents the absolute distance between the chosen pair of TMs at the $(n-1)$th frame, and N is the total number of frames in the recording. Because of the framework introduced in (2), D_{n-1} remains equal to D_1. As a result, (3) provides an estimate that is related to the Lagrangian strain.

From our observations, UP was not the only source of motion influencing the movement of the endometrium in TVUS recordings. Other motions, either coming from different organs, such as bowels and bladder, or caused by heartbeat, respiration, and probe movement during the acquisition, were all recorded during the US scan. Therefore, a bandpass filter was applied to the RSR signals to remove the interference from these undesired motion sources.

From the literature, UP during a normal menstrual cycle varies from 0.5 to 4.1 contractions per minute [25], while during IVF treatment, UP appears to show higher frequencies due to the ovarian stimulation, resulting in a range from 0.5 to 5 contractions per minute [12], [26]. The cutoff frequencies of the bandpass filter were therefore set according to the literature based on the application.

E. Feature Extraction

In this study, we focused on analyzing the velocity, direction, and coordination of the UP, which might have a direct impact on the success of pregnancy.

Based on the RSR signals, we created a time–space representation of the UP waves propagating along with the endometrium, as shown in Fig. 4(a) and (b). The RSR signals are aligned in space from the cervix to fundus (y-axis) based on the distance between each pair of TMs. The x-axis represents the time evolution of RSR signals, and the color code represents the value of the RSR signals. Positive RSR, shown in yellow, indicates uterine relaxation, while negative RSR, shown in blue, indicates uterine contraction. Clear UP propagation from cervix to fundus (C2F) and from fundus to cervix (F2C) can be observed in Fig. 4(a) and (b), respectively.

1) UP Velocity: A moving window, including 600 frames (20 s), was applied to segment the time–space representation over time. This duration allows including at least one full UP wave cycle in the time window. Within each segment, 2-D fast Fourier transform was applied to the time–space representation, providing a frequency representation in the k-space domain. UP velocities in both C2F and F2C directions can be explicitly estimated from the peaks in the first quadrant (representing C2F propagation) and the second quadrant (representing F2C propagation) of the k-space.

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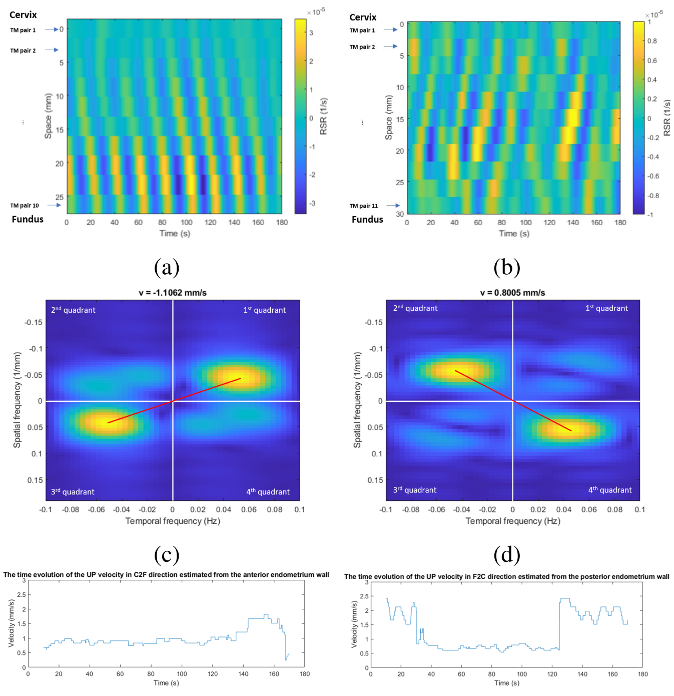

Fig. 4. (a) UP time–space representation based on the RSR extracted from the anterior wall of the endometrium from a healthy volunteer. This plot shows clear propagation C2F. (b) UP time–space representation based on the RSR extracted from the posterior wall of the endometrium from a healthy volunteer. This plot presents the F2C propagation. (c) Corresponding *k*-space representation of (a): dominant spectral peaks (marked with red points) are present in the first and third quadrant representing C2F propagation. (d) Corresponding *k*-space representation of (b): dominant spectral peaks (marked with red points) are present in the second and fourth quadrant representing F2C propagation. (e) Time evolution of the UP velocity in the C2F direction estimated from (a). (f) Time evolution of the UP velocity in the F2C direction estimated from (b).

Fig. 4(a) and (b) shows the frequency representations of Fig. 4(a) and (b) within one of the moving windows ($t = 40$–60 s). The evolution of UP velocities in both directions is shown in Fig. 4(e) and (f).

The temporal and spatial frequencies of the dominant peristaltic motion were identified at the peaks of the spectrum. The corresponding UP velocity, v_{UP}, was then calculated as the ratio between the temporal frequency, f_t, and spatial frequency, f_x as

$$v_{\mathrm{UP}} = \frac{f_t}{f_x}. \tag{4}$$

2) UP Direction: Theoretically, the direction of the propagation can be determined by the sign of v_{UP}. Propagation from C2F is here indicated by a positive sign, while propagation from F2C is indicated by a negative sign. However, as discussed in [9] and [11], more complex UP patterns can also be observed. Opposing propagation, which shows both C2F and F2C propagation, is often observed after ovulation to support embryo implantation; recoiling propagation, which consists of reflection and superposition of multiple peristaltic waves, can also be observed, as well as more complex propagation. Fig. 5(a) shows an example of a complex propagation pattern during the EL phase.

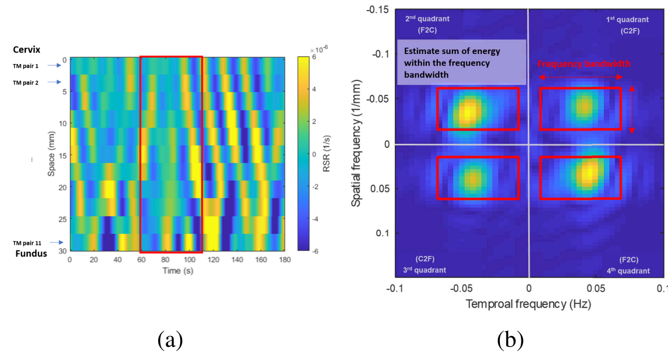

Fig. 5. (a) Time–space representation of a complex UP pattern. The direction of UP propagation changes from F2C to C2F during the acquisition (highlighted in the red area). (b) *K*-space representation of the UP. The sum of the spectral energies estimated within the physiological bandwidth from the first and third quadrants represents the energy of C2F propagation; the sum of the spectral energies estimated within the physiological bandwidth from the second and fourth quadrants represents the energy of F2C propagation.

Simple binary classification based on the sign of v_{UP} is not suitable when a complex propagation pattern occurs. Therefore, we propose an energy ratio (ER) metrics, where the sum of spectral energies is estimated from the first quadrant ($E1$) and the second quadrant ($E2$), representing the energy of C2F and F2C propagation, respectively [see Fig. 5(b)]. This is given as

$$\mathrm{ER} = 2 \times \frac{E1}{E1 + E2} - 1. \tag{5}$$

The parameter ER is comprised between -1 and 1. In this study, we conventionally assumed $\mathrm{ER} > 0.1$ to indicate C2F propagation and otherwise for $\mathrm{ER} < -0.1$. ER around zero indicates the presence of opposing or "standing" waves.

To estimate the global propagation direction, $E1$ and $E2$ were estimated on the full recording rather than within the moving window adopted for the estimation of the UP velocity.

F. UP Coordination

The fact that locally, e.g., along the anterior or posterior wall, UP shows a dominant direction, does not guarantee an effective peristaltic movement that is coordinated and generates microstreaming in the endometrial cavity. Simply focusing on the anterior and posterior walls, coordinated, effective peristalsis requires UP propagation on both sides of the endometrium to show the same direction at the same time. Especially before ovulation, muscles from both sides of the endometrium have to produce coordinated contractions to support sperm transport from the vagina to the fallopian tubes, where fertilization occurs [25], [27].

Similar time evolution of the ER is expected from both the anterior ($\mathrm{ER}_{\mathrm{ant}}$) and posterior ($\mathrm{ER}_{\mathrm{pos}}$) walls of the endometrium that are expected. Similarity measures, namely, cross correlation (CC), mean squared error (MSE), and Hausdorff distance (Hd) [17], [28], were therefore employed as cost functions to assess the spatiotemporal coordination of the UP.

III. Validation Strategy

In vitro and *in vivo* validations were performed to test the ability of the proposed method to measure and characterize

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UP. *In vitro*, we optimized the parameterization and verified the accuracy of the OF with the data acquired by a dedicated setup with an *ex vivo* uterus introduced in [17]. *In vivo*, the proposed method was validated with TVUS recordings acquired in healthy volunteers during their normal menstrual cycle and in patients undergoing IVF treatment.

A. Validation in Healthy Volunteers

According to previous studies [9], [25], the uterus presents different behavior in different phases of the menstrual cycle, showing different contraction frequencies and velocities. Therefore, we validated our proposed method for its ability to characterize and distinguish different UP patterns along the natural menstrual cycle.

1) Feature Extraction: After deriving the RSR from the tracking results, UP velocities in both C2F and F2C directions were calculated inside the moving window. After that, median velocities (MVs) in C2F and F2C directions were calculated by averaging velocities over time in the corresponding directions. The MSE, CC, and Hd between ER_{ant} and ER_{pos} were also estimated from each RSR signal to assess the UP coordination in each phase. The global propagation direction represented by ER metric was explicitly calculated on the full recording without the moving window.

2) Intraobserver and Interobserver Study: To validate the reproducibility of our method, we conducted an intraobserver study. The TMs were positioned by the same operator in two subsequent 4-min recordings acquired from the same healthy volunteer.

To further analyze the intraobserver variability, the TMs were positioned three times by the same operator in the same set of recordings. In addition, two clinicians were also asked to place the TMs on the same set of recordings to perform an interobserver variability test after a 10-min training.

Intraclass coefficient (ICC) was used to determine the agreement between the features extracted from different measurements.

ICC was calculated by using IBM SPSS Statistics 27. A two-way mixed model with index type of absolute agreement was employed to verify the reliability of our measures on UP velocities and coordination. $ICC > 0.5$ was considered as moderate agreement, $ICC > 0.75$ was considered a good agreement, and $ICC > 0.9$ was considered an excellent agreement [29].

3) Statistical Analysis: It was performed using MATLAB 2018b. The Shapiro–Wilk test was first applied to test the normality of the distributions. A one-way analysis of variance test with Duncan test as *post hoc* (in case of Gaussian distribution) or Kruskal–Wallis test with Dunn–Sidak test as *post hoc* (in case of non-Gaussian distribution) was applied. MV, as well as the coordination features CC and MSE, was tested to discriminate among the four selected phases. A p-value < 0.05 was considered statistically significant.

B. Validation in IVF Patients

Validation in IVF patients aimed at testing the ability of the extracted features to distinguish between the successful and unsuccessful groups following IVF. Features that can establish significant differences between the two groups can be considered as predictors of successful IVF treatment. In all patients, only top-quality embryos, according to morphological analysis, were transferred.

1) Feature Extraction: The MV of the UP in both C2F and F2C directions, as well as the coordination between ER_{ant} and ER_{pos} by CC, MSE, and Hd, was calculated from each RSR signal in each patient.

2) Statistical Analysis: Double-tailed Student's t-test (in case of Gaussian distribution) or Wilcoxon rank-sum test (in case of non-Gaussian distribution) was used. A p-value < 0.05 was considered statistically significant.

IV. Results

All results are reported in the format of median (quartiles 1–3).

A. Validation in Healthy Volunteers

Forty-four TVUS recordings from 11 healthy volunteers during the four different phases of the menstrual cycle were originally planned. However, due to dropout of some subjects, two during Menses and one during LF, a total number of 41 TVUS recordings were eventually available for the analysis. These recordings underwent a quantitative quality check as introduced in Section II-C. Based on this, five additional recordings (two during Menses, one during EL, and two during LF) were excluded. Therefore, a total of 36 TVUS recordings (seven during Menses, eight during LF, ten during EL, and 11 during LL) were processed and contributed to our statistical analysis.

Fig. 6(a) shows the MV in C2F and F2C direction extracted from the four selected phases of a normal menstrual cycle. From Menses to the LF phase, the MV in C2F direction increases from 0.72 (0.48–0.77) to 0.76 (0.63–0.96) mm/s, while it decreases to 0.71 (0.67–0.85) mm/s in the EL phase and 0.50 (0.49–0.61) mm/s in the LL phase. The MV in the F2C direction shows the same trend, with values of 0.66 (0.46–0.74) mm/s during Menses, 0.93 (0.56–1.31) mm/s in the LF phase, 0.75 (0.68–0.88) mm/s in the EL phase, and 0.52 (0.41–0.60) mm/s in the LF phase. In particular, the MV in the C2F direction shows a significant difference between the LF phase and the LL phase ($p = 0.0130$) and between the EL and the LL phases ($p = 0.0473$). Instead, the MV in the F2C direction shows a significant difference between the LF and the LL phases ($p = 0.0183$) and between the EL and the LL phases ($p = 0.0205$).

Fig. 6(b) shows the direction of UP propagation among the selected four phases of the menstrual cycle. During Menses, UP propagation is mostly in the F2C direction. In the LF phase, dominant C2F or F2C propagation can be observed, and a similar behavior also appears in the EL phase. Finally, in the LL phase, no F2C propagation but mostly "standing"/opposing propagation can be observed.

Considering the coordination feature, a trend toward higher CC [0.29 (−0.10 to 0.38)] was found in the Menses phase, and

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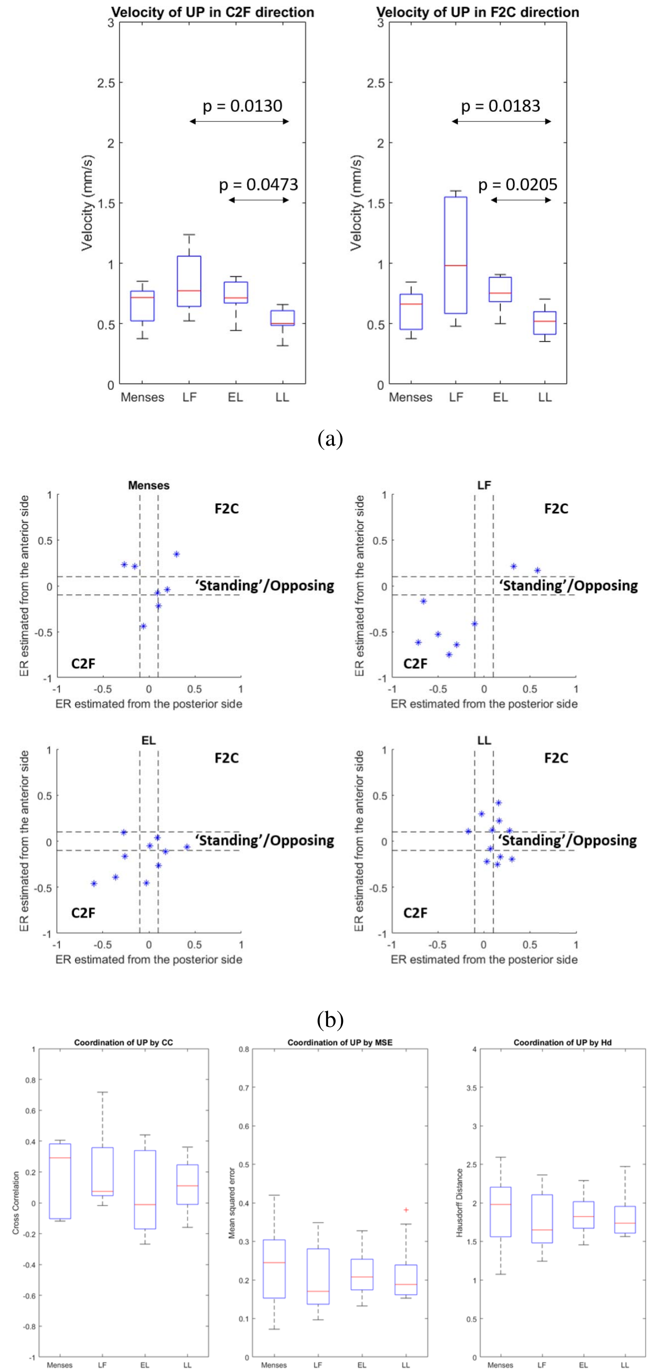

Fig. 6. Velocity, direction, and coordination results obtained from 36 TVUS recordings acquired during four phases of the menstrual cycle (seven during Menses, eight during LF, ten during EL, and 11 during LL) from healthy volunteers. (a) Box plots reporting the statistical results for the UP MV extracted from the RSR signals along the C2F and F2C directions. The asterisk (*) indicates a significant difference ($p < 0.05$) between different phases. (b) Direction results based on the ER metrics estimated from the anterior (y-axis) and posterior (x-axis) walls of the endometrium. (c) Coordination results based on CC, MSE, and Hd.

a trend toward lower MSE [0.17 (0.14–0.28)] and Hd [1.65 (1.48–2.10)] was both found in the LF phase [see Fig. 6(c)].

In total, ten pairs of TVUS recordings (one during Menses, three during LF, one during EL, and five during LL) were available that passed the quantitative quality check. ICC and its 95% confidence interval of the extracted features are reported in Tables I and II.

TABLE I

INTRAOBSERVER REPRODUCIBILITY TEST: UP VELOCITY AND COORDINATION FEATURES WERE EXTRACTED FROM TWO SUBSEQUENT TVUS RECORDINGS ACQUIRED FROM TEN HEALTHY VOLUNTEERS. ICC AND ITS 95% CONFIDENCE INTERVAL OF THE EXTRACTED FEATURES ARE REPORTED

Feature name	ICC	95 % Confidence Interval	
		Lower Bound	Upper Bound
Velocity C2F	0.918	0.689	0.979
Velocity F2C	0.961	0.798	0.991
Coordination by CC	0.950	0.771	0.988
Coordination by MSE	0.914	0.673	0.978
Coordination by Hd	0.899	0.602	0.975

TABLE II

INTRAOBSERVER AND INTEROBSERVER VARIABILITY TEST: UP VELOCITY AND COORDINATION FEATURES WERE EXTRACTED FROM TVUS RECORDINGS ACQUIRED FROM TEN HEALTHY VOLUNTEERS. ICC (95% CONFIDENCE INTERVAL) OF THE EXTRACTED FEATURES IS CALCULATED AMONG THREE TRAILS (INTRAOBSERVER) AND THREE OPERATORS (INTEROBSERVER)

Feature name	ICC	
	Intra-observer variability	Inter-observer variability
Velocity C2F	0.969 (0.910 - 0.992)	0.953 (0.866 - 0.987)
Velocity F2C	0.921 (0.762 - 0.979)	0.965 (0.899 - 0.990)
Coordination by CC	0.853 (0.589 - 0.960)	0.752 (0.318 - 0.931)
Coordination by MSE	0.841 (0.553 - 0.956)	0.762 (0.353 - 0.934)
Coordination by Hd	0.863 (0.616 - 0.963)	0.785 (0.409 - 0.940)

B. Validation in IVF Patients

In total, 81 TVUS recordings (65 from the IMPLANT 1 study and 16 from Ghent University Hospital) were acquired from IVF patients 1 h before ET; 20 TVUS recordings from the IMPLANT 1 study had to be excluded because of improper imaging windows. The remaining 61 TVUS recordings underwent the proposed quantitative quality check, by which additional 11 TVUS recordings from the IMPLANT 1 study were excluded. All 16 TVUS recordings acquired at Ghent University Hospital passed the quality check. In the end, in total, 50 TVUS recordings were included for further analysis. Sixteen out of the selected 50 patients got pregnant after the treatment, while the remaining 34 failed.

The UP MV in the C2F direction 1 h before ET was 0.51 (0.45 to 0.65) mm/s in the success group and 0.63 (0.57 to 0.74) mm/s in the failure group. When considering the C2F direction, the MV values were equal to 0.56 (0.52–0.65) mm/s in the successful group and 0.70 (0.61–0.74) mm/s in the unsuccessful group [see Fig. 7(a)]. Significantly higher velocities in the C2F ($p = 0.0082$) and F2C ($p = 0.0073$) directions were found in the failure group compared to the success group.

As shown in Fig. 7(b), the global direction features extracted from both the successful and unsuccessful pregnancy groups do not show different distributions and are scattered across all categories.

Considering the coordination features, higher CC [0.26 (0.04–0.38)], lower MSE [0.20 (0.16–0.30)], and lower Hd

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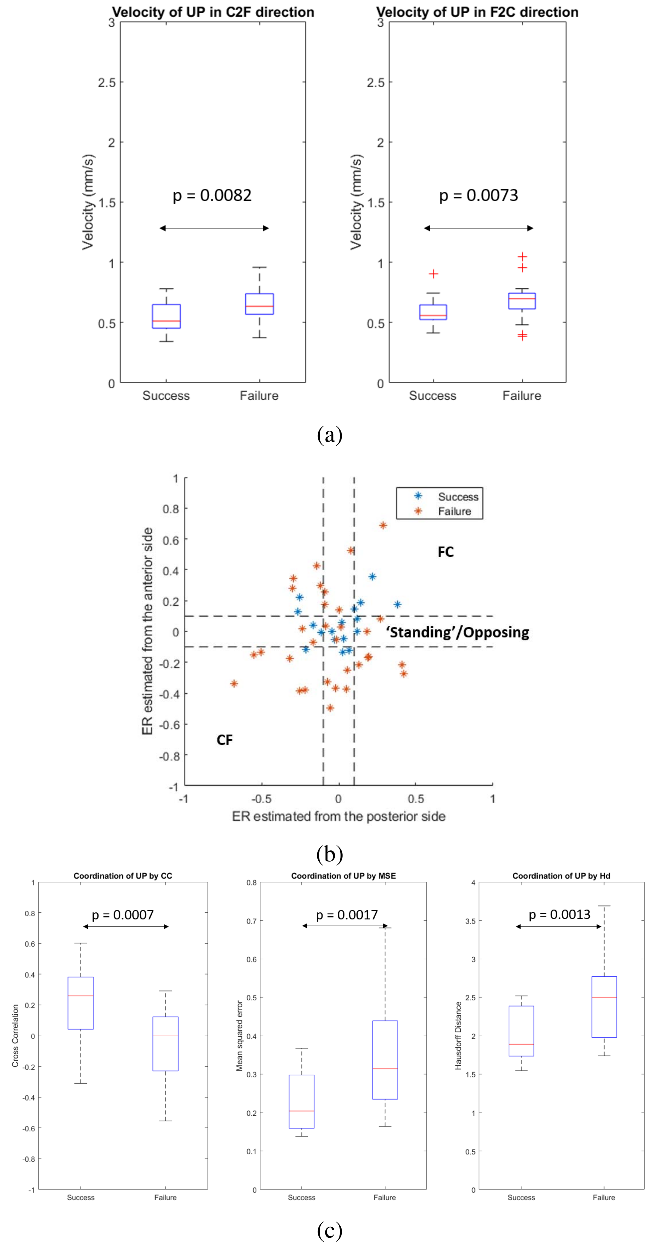

Fig. 7. Velocity, direction, and coordination results obtained from 50 IVF patients are illustrated as follows: (a) Box plots reporting the statistical results for the UP MV extracted from the RSR signals along the C2F and F2C directions. (b) Direction results based on ER metrics estimated from the anterior (y-axis) and posterior (x-axis) walls of the endometrium. (c) Coordination results based on CC, MSE, and Hd. The asterisk (*) indicates a significant difference ($p < 0.05$) between successful and unsuccessful groups.

[1.89 (1.73–2.39)] were found in the success group compared to the failure group [CC $= 0.00$ (from -0.23 to 0.13), MSE $= 0.31$ (0.23–0.44), and Hd $= 2.50$ (1.98–2.77)] [see Fig. 7(b)]. The differences were statistically significant for all coordination features: CC ($p = 0.0006$), MSE ($p = 0.0017$), and Hd ($p = 0.0013$).

V. Discussion

A. Validation in Healthy Volunteers

1) Estimation of UP Velocity, Direction, and Coordination: The trend of the UP velocity changes across the selected menstrual phases is well aligned with the observation of Ijland *et al.* [10]. In the LL phase, which is the most quiescent phase during the entire menstrual cycle, the visualization of UP is challenging. Thus, from manual observation, no UP is reported. However, with our proposed method, the velocities of the UP in both directions could still be assessed. Besides, significant differences in the velocity of UP propagation were found between LF and LL phases and between EL and LL phases in both C2F and F2C directions. These findings are in agreement with previous literature reporting different behavior of the uterus in the different phases of a natural menstrual cycle [9], [25].

Our findings on UP direction are in agreement with our clinical expectations and the findings from other qualitative studies [25], [30]. For instance, during Menses, intrauterine streams were expected to be generated mainly in the F2C direction for menstrual emptying, and in the LF phase, pure one-directional propagation was anticipated.

No significant difference was found based on the coordination features among the four selected phases during the menstrual cycle. However, a trend of higher UP coordination was found during the LF phase, which may correspond to the generation of coordinated contractions favoring sperm transport from the vagina to the orifices of the fallopian tubes, where fertilization occurs [25], [27].

2) Intraobserver and Interobserver Study: According to the ICC results from the intraobserver reproducibility study (see Table I), excellent agreements were found for most of the features, indicating good reproducibility and robustness of our proposed method. We also observed excellent agreement for the velocity features, and good agreement for the coordination features from the intraobserver and interobserver variability studies. Since the coordination features required a good spatial alignment of the TMs positioned at both sides of the endometrium, posing extra challenge on the new users, the interobserver variability was slightly worse than the intraobserver variability. This can be further improved by either conducting a more detailed TM positioning protocol for user guidance or investigating automatic segmentation techniques.

The ability to quantify and characterize the uterine activity with the proposed method can also aid the diagnosis of uterine dysfunction and diseases. This will be investigated in future dedicated studies.

B. Validation in IVF Patients

1) Estimation of UP Velocity, Direction, and Coordination: Significantly higher velocities in both directions were found in the failure group compared to the success group. However, if we compare the velocities in the F2C direction extracted 1 h before ET and during the LF phase from healthy volunteers, the results are very similar. This finding suggest that, even though these patients are suffering from infertility problems and treated with hormones, the UP velocity is similar to that in healthy women in a comparable phase of the menstrual cycle.

Our findings also suggest UP direction to be a poor predictor of the success of embryo implantation. This result may be

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ascribed to the complex propagation patterns observed before embryo implantation in both the successful and unsuccessful pregnancy groups.

Significant differences in UP coordination were found between the success and failure groups from all metrics. Well-coordinated UP (higher CC and lower Hd and MSE) was found in the success group. This result suggests that proper coordination of uterine muscle contraction may be a relevant factor determining successful embryo implantation.

C. Study Limitations

This feasibility study was carried out with a limited dataset. To confirm the predictive value of the proposed features, larger datasets should be acquired and investigated in the future. The analysis of larger datasets would then benefit from automatic segmentation of the uterus, reported, e.g., in [31], enabling fully automatic positioning of the TMs rather than the semiautomatic approach employed in this study.

Twenty out of 81 TVUS recordings from IVF patients had to be excluded because of improper imaging window. These were all part of the retrospective IMPLANT 1 study, while no recording had to be excluded from the prospective Ghent study. This suggests the relevance of instructing the sonographers on the acquisition requirements.

The proposed speckle tracking method is based on TVUS B-mode images. This approach has the advantage of being easily transferred to different ultrasound scanners, However, more accurate results can in principle be obtained by the employment of the raw radio frequency (RF) signals, although conflicting results are reported [32]. In future work, when access to the RF signals is available, speckle tracking based on RF signals could be implemented and evaluated.

In this study, the TMs were positioned in the junctional zone close to the subendometrial line, which is the region where UP is mostly observed. However, from a physiological perspective, uterine motion should be mostly ascribed to myometrial cells [33]. Therefore, the initial positions of the TMs might have an impact on the UP characterization in relation to the physiological structure of the uterus. As we only investigated the UP characteristics close to the endometrium within the junctional zone, it would be interesting in the future to extend the investigation to the myometrium, where uterine motion originates, to obtain a more comprehensive analysis of UP.

D. Future Perspective

Our proposed method for uterine strain analysis is designed to keep constant distances between the TMs over time and good alignment with the uterine anatomy while mitigating the effect of decorrelation due to OOP motion. These conditions enable our proposed spatial–temporal analysis. However, strong in-plane deformation of the endometrium might in principle lead to misalignment between the endometrial walls and the TM grid. To overcome these problems, automatic segmentation of the endometrial walls may be considered in the future [31], [34], possibly enabling improved grid placement and strain rate localization with respect to the uterine anatomy.

The promising novel features for the characterization of different uterine activity and associated UP patterns, such as UP velocity and coordination, have been introduced in this study. In the future, these features can be integrated into a machine learning framework with additional standard features, such as contraction frequency and amplitude, to further improve the prediction of successful embryo implantation [18]. With this approach, clinicians could be supported with critical decision-making, such as whether to proceed with the ET or to freeze the embryo and wait for more favorable UP characteristics. In this way, increased IVF success rates may be possibly achieved. To test this hypothesis, dedicated clinical trials should be performed where predictive modeling and subsequent decisions are integrated into the clinical workflow.

The mechanical activity of the uterus is not the only determinant of successful IVF. Extensive research has focused on the assessment of embryo quality as a predictor of successful embryo implantation [35]. Also, in this context, predictive models based on machine learning are being developed and investigated [36]. In addition, it is worth investigating the relationship between patient responses to hormone injection and related changes in UP characteristics. The combination of features reflecting embryo quality, hormone response, and UP characteristics can be envisaged to improve the prediction of IVF success throughout a machine learning model.

In this work, 2-D TVUS recordings were all acquired in the sagittal plane, and the main focus was on measuring the uterine contraction in the radial direction. However, with the advent of 3-D US options, complex UP patterns and OOP motion can be analyzed and elucidated accounting for all spatial dimensions. This will also contribute to improve our knowledge of the uterine dynamics by exploring its longitudinal and circumferential deformation, opening up new possibilities for characterizing UP and understanding the underlying physiological processes.

Although this study focused on IVF, UP assessment and characterization can represent a valuable diagnostic tool also in the context of widespread pathological conditions of the uterus, such as adenomyosis and endometriosis, which may be reflected in altered UP patterns. Dedicated clinical trials can be designed in the future to investigate the potential of the proposed features for the diagnosis of uterine diseases and dysfunctions.

VI. Conclusion

A new method for quantitative analysis and characterization of UP based on ultrasound speckle tracking is proposed. Features related to the velocity, direction, and coordination of the peristaltic waves are extracted and successfully evaluated for their ability to differentiate between the different phases of a natural menstrual cycle as well as to predict the success of *in vitro* fertilization. Our promising results open up new possibilities for improving the success rates of *in vitro* fertilization treatment as well as for improving our understanding of the physiological mechanisms underlying UP, which is still poorly comprehended.

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REFERENCES

[1] J. Boivin, L. Bunting, J. A. Collins, and K. G. Nygren, "International estimates of infertility prevalence and treatment-seeking: Potential need and demand for infertility medical care," *Hum. Reprod.*, vol. 22, no. 6, pp. 1506–1512, Jun. 2007.

[2] A. Andersen *et al.*, "Assisted reproductive technology in Europe, 2001. Results generated from European registers by ESHRE," *Hum. Reproduction*, vol. 20, no. 5, pp. 1158–1176, May 2005.

[3] C. De Geyter *et al.*, "Corrigendum. ART in Europe, 2015: Results generated from European registries by ESHRE," *Hum. Reproduction Open*, vol. 2020, no. 3, pp. 1586–1601, Mar. 2020.

[4] R. Fanchin and J. M. Ayoubi, "Uterine dynamics: Impacton the human reproduction process," *Reproductive Biomed. Online*, vol. 8, no. Suppl. 2, pp. S57–S62, 2009, doi: 10.1016/S1472-6483(10)60450-6.

[5] L. Zhu, H. S. Che, L. Xiao, and Y. P. Li, "Uterine peristalsis before embryo transfer affects the chance of clinical pregnancy in fresh and frozen-thawed embryo transfer cycles," *Hum. Reproduction*, vol. 29, no. 6, pp. 1238–1243, Jun. 2014.

[6] N. P. M. Kuijsters, W. G. Methorst, M. S. Q. Kortenhorst, C. Rabotti, M. Mischi, and B. C. Schoot, "Uterine peristalsis and fertility: Current knowledge and future perspectives: A review and meta-analysis," *Reproductive Biomed. Online*, vol. 35, no. 1, pp. 50–71, 2017.

[7] M. M. Ijland, J. L. H. Evers, G. A. J. Dunselman, L. Volovics, and H. J. Hoogland, "Relation between endometrial wavelike activity and fecundability in spontaneous cycles," *Fertility Sterility*, vol. 67, no. 3, pp. 492–496, Mar. 1997.

[8] R. L. Dickinson, "The technic of timing human ovulation by palpablechanges in ovary, tube, and uterus," *Amer. J. Obstetrics Gynecol.*, vol. 33, no. 6, pp. 1027–1033, 1937.

[9] I. van Gestel, M. M. Ijland, H. J. Hoogland, and J. L. H. Evers, "Endometrial wave-like activity in the non-pregnant uterus," *Hum. Reproduction Update*, vol. 9, no. 2, pp. 131–138, Mar. 2003, doi: 10.1093/humupd/dmg011.

[10] M. M. IJland, J. L. Evers, and H. J. Hoogland, "Velocity of endometrial wavelike activity in spontaneous cycles," *Fertility Sterility*, vol. 68, no. 1, pp. 72–75, Jul. 1997.

[11] J. C. Birnholz, "Ultrasonic visualization of endometrial movements," *Fertility Sterility*, vol. 41, no. 1, pp. 157–158, Jan. 1984.

[12] R. Fanchin, C. Righini, F. Olivennes, S. Taylor, D. de Ziegler, and R. Frydman, "Uterine contractions at the time of embryo transfer alter pregnancy rates after *in vitro* fertilization," *Human Reproduction*, vol. 13, no. 7, pp. 1968–1974, Jul. 1998.

[13] N. P. M. Kuijsters, F. Sammali, C. Rabotti, Y. Huang, M. Mischi, and B. C. Schoot, "Visual inspection of transvaginal ultrasound videos to characterize uterine peristalsis: An inter-observer agreement study," *J. Ultrasound*, vol. 23, no. 1, pp. 37–44, Feb. 2019.

[14] F. Sammali *et al.*, "Dedicated ultrasound speckle tracking for quantitative analysis of uterine motion outside pregnancy," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 66, no. 3, pp. 581–590, Mar. 2019.

[15] Y. Zhou and Y.-P. Zheng, "A motion estimation refinement framework for real-time tissue axial strain estimation with freehand ultrasound," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 57, no. 9, pp. 1943–1951, Sep. 2010.

[16] J. Bouguet, "Pyramidal implementation of the affine Lucas Kanade feature tracker," Tech. Rep., 2001. [Online]. Available: http://robots.stanford.edu/cs223b04/algo_tracking.pdf

[17] F. Sammali *et al.*, "Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking," *Biomed. Phys. Eng. Exp.*, vol. 4, no. 3, Mar. 2018, Art. no. 035012.

[18] F. Sammali *et al.*, "Prediction of embryo implantation by machine learning based on ultrasound strain imaging," in *Proc. IEEE Int. Ultrason. Symp. (IUS)*, Oct. 2019, pp. 1141–1144.

[19] G. Griesinger *et al.*, "Effect of the oxytocin receptor antagonist nolasiban on pregnancy rates in women undergoing embryo transfer following IVF: Analysis of three randomised clinical trials," *Hum. Reproduction*, vol. 36, no. 4, pp. 1–14, Feb. 2021.

[20] B. Balaban *et al.*, "The Istanbul consensus workshop on embryo assessment: Proceedings of an expert meeting," *Hum. Reprod.*, vol. 26, no. 6, pp. 1270–1283, 2011.

[21] C. Blank *et al.*, "Prediction of implantation after blastocyst transfer in *in vitro* fertilization: A machine-learning perspective," *Fertility Sterility*, vol. 111, no. 2, pp. 318–326, Feb. 2019.

[22] B. Lucas and T. Kanade, "An iterative image registration technique with an application to stereo vision," in *Proc. Int. Joint Conf. Artif. Intell.*, vol. 2, 1981, pp. 674–679.

[23] S. Novellas *et al.*, "MRI characteristics of the uterine junctional zone: From normal to the diagnosis of adenomyosis," *Amer. J. Roentgenol.*, vol. 196, no. 5, pp. 1206–1213, May 2011.

[24] J. L. Rodgers and W. A. Nicewander, "Thirteen ways to look at the correlation coefficient," *Amer. Statistician*, vol. 42, no. 1, pp. 59–66, Feb. 1988, doi: 10.1080/00031305.1988.10475524.

[25] C. Bulletti, D. de Ziegler, V. Polli, L. Diotallevi, E. D. Ferro, and C. Flamigni, "Uterine contractility during the menstrual cycle," *Hum. Reproduction*, vol. 15, no. suppl. 1, pp. 81–89, Jun. 2000.

[26] R. Fanchin, "Uterine contractility decreases at the time of blastocyst transfers," *Hum. Reproduction*, vol. 16, no. 6, pp. 1115–1119, Jun. 2001.

[27] M. M. Ijland, G. A. Dunselman, H. Hoogland, and J. L. H. Evers, "Subendometrial contractions in the nonpregnant uterus: An ultrasound study," *Eur. J. Obstetrics Gynecol. Reproductive Biol.*, vol. 70, no. 1, pp. 23–24, 1996.

[28] D. P. Huttenlocher, G. A. Klanderman, and W. J. Rucklidge, "Comparing images using the Hausdorff distance," *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. 15, no. 9, pp. 850–863, Sep. 1993.

[29] T. K. Koo and M. Y. Li, "A guideline of selecting and reporting intraclass correlation coefficients for reliability research," *J. Chiropractic Med.*, vol. 15, no. 2, p. 155, Jun. 2016.

[30] G. Kunz and G. Leyendecker, "Uterine peristaltic activity during the menstrual cycle: Characterization, regulation, function and dysfunction," *Reproductive Biomed. Online*, vol. 4, pp. 5–9, Jan. 2002.

[31] R. Supriyanti, D. A. Putri, E. Murdyantoro, and H. B. Widodo, "Comparing edge detection methods to localize uterus area on ultrasound image," in *Proc. 3rd Int. Conf. Instrum., Commun., Inf. Technol. Biomed. Eng. (ICICI-BME)*, Nov. 2013, pp. 152–155.

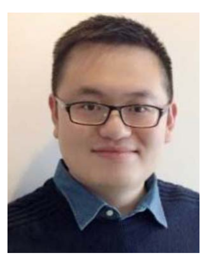
[32] J. Steinbuch, A. P. G. Hoeks, E. Hermeling, M. T. B. Truijman, F. H. B. M. Schreuder, and W. H. Mess, "Standard B-mode ultrasound measures local carotid artery characteristics as reliably as radiofrequency phase tracking in symptomatic carotid artery patients," *Ultrasound Med. Biol.*, vol. 42, no. 2, pp. 586–595, Feb. 2016.

[33] R. Young, "Myocytes, myometrium, and uterine contractions," in *Annals of the New York Academy of Sciences*, vol. 1101. Oxford, U.K.: Blackwell, Apr. 2007, pp. 72–84. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/17442780

[34] N. Singhal, S. Mukherjee, and C. Perrey, "Automated assessment of endometrium from transvaginal ultrasound using deep learned snake," in *Proc. IEEE 14th Int. Symp. Biomed. Imag. (ISBI)*, Apr. 2017, pp. 283–286.

[35] T. Ebner, "Selection based on morphological assessment of oocytes and embryos at different stages of preimplantation development: A review," *Hum. Reproduction Update*, vol. 9, no. 3, pp. 251–262, May 2003.

[36] C. Blank *et al.*, "Assessment of uterine activity during IVF by quantitative ultrasound imaging: A pilot study," *Reproductive Biomed. Online*, vol. 41, no. 6, pp. 1045–1053, Dec. 2020.



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