Prediction of Fertile Window Using a Contact-Free Under-the-Mattress Sensor

Abstract

The purpose of the presented study was to evaluate the performance of a novel contact-free under-the-mattress sensor in prediction of women’s fertile window (FW), at home environment. 30 normal-ovulatory women at the age of 22-40 years took part in the study. Heart rate, heart rate variability, and respiration rate values were measured during a period of 3-6 months. These measurements were recorded at the home environment, during night time, using a contact free sensor positioned under the participant’s mattress. Predictions of the FW were obtained using an algorithm based on the sensor measurements and menses dates, as reported by the participants. For each participant, and each cycle, the ground-truth ovulation day was established by daily blood tests to measure hormone levels (LH, estrogen, and progesterone), and transvaginal ultrasound scans to determine follicle size. The accuracy of the sensor FW prediction was calculated as the overlap between the ground-truth and predicted FW (based on sensor's measurements). Comparison were also made to standard methods of FW prediction, which relies on the duration of a woman's previous menstrual cycles.

Overall, a total of 216 menstrual cycles were recorded. Predicted FW overlapped 61.3 % ± 4.9 % of ground truth after the first menstrual cycle and 72.2 % ± 5.1 % after three menstrual cycles. Prediction overlap as obtained by the standard method was 53.0 % ± 6.9 % after the first menstrual and reached 63.3 % ± 6.3 % after three menstrual cycles.

The results suggest that the use of a contact free sensor enhances the ability to accurately predict the FW as defined by the expert reference. Alternative available methods for fertility prediction, require the user to follow a strict protocol, such as measuring basal body temperature or urine LH levels, on a daily basis at morning time. The new contact free sensor requires minimal compliance from the user and increases the chances to conceive, compared to the standard prediction method based only on the duration of menstrual cycles.

1. Introduction

Correctly identifying the fertile window (FW) could play a crucial role for those who attempt to conceive. Nevertheless, as its timing and length may vary within and between individuals, it was proven hard to determine in any given instance when the FW occurs (or will occur) and how long is it [1]. For that, there are many methods aiming to detect FW. The most accurate and validated techniques require medical examination (i.e., transvaginal ultrasound and tracking reproductive hormones using blood tests). However, the rate of success and precision decreases rapidly and complexity increases as the woman leaves the clinic and attempts to identify her approaching FW independently, often depends on her compliance and precise use. Popular methods range from prediction of ovulation day based on average cycle length and the assumption of constant luteal phase duration, to daily measurements that try to measure physiological changes such as body temperature at the end of the night (Basal Body Temperature, BBT) or observation of cervical mucus or tracking the luteinizing hormone (LH) level changes using a daily urinary test [2]. These methods require compliance, are frequently cumbersome, and their results are comparably low [3]. For example, detection of rise in BBT or LH indicate the end of the FW and might be too late to allow for successful conception.

Evidence suggest the involvement of different reproductive hormones in the cardiovascular system changes [4, 5], mainly the progesterone and estrogen. Heart rate (HR), respiratory rate (RR) as well as heart rate variability (HRV) tend to oscillate throughout the different menstrual phases [6, 7]. HR rises during the luteal phase, presumably due to the corresponding progesterone surge which affects basal body temperature. RR is relatively low during the end of the follicular phase and the ovulation phase and increases toward the menses. Similarly, the high frequency (HF) variability of the HR during sleep follows the same pattern, i.e. comparatively low during the ovulation phase and rises toward the menses.

Furthermore, relationship between the menstrual cycle and cardiovascular activity were also found during sleep. For example, it was shown that the HF component of the HRV is lower during the mid-luteal phase, compared to the late-luteal and follicular phases in both rapid eye movement (REM) and non-REM sleep stages [8]. In addition, HR was relatively higher in the mid-luteal phase, compared to the late-luteal and follicular phases during sleep.

The time of sleep, and even more specific, the end of the night, is considered to be a time in which the body is in 'baseline mode', thus, any effect of previous day's activity, e.g., eating, drinking, sport activity, stress of any kind, is thought to be reduced to minimum. This may be the reason that trying to predict the FW by measuring cardiovascular
performance during daytime led to mixed results and that existing in-home methods and solutions target the measurements to the end of the night.

Ideally, a preferred solution for tracking the menstrual cycle at home entails a solution that is as automated as possible, measures baseline at the night, and removes the compliance issue. Recently, a study that tried to meet these requirements tracked the woman's HR using a wearable device (a photoplethysmographic sensor, located on the wrist) and found a significant HR differences between different time periods within the menstrual cycle, specifically, the time of ovulation, the mid-luteal term and the menses [9]. While the above study utilized a wearable device that requires some compliance of actually wearing the device to bed every night, EarlySense has developed a contactless fertility cycle monitoring device that is placed under the mattress and continuously monitors HR, RR, HRV and other sleep parameters [10]. The system includes a piezoelectric sensor that is installed once under the bed mattress and in no way contacts the person in bed. A software package downloadable on a smartphone or tablet analyses the recorded physiological signals, tracks the woman's cardiovascular activity, and uses this information to calculate her fertility cycle.

The aim of the current study was to establish the accuracy of the predicted FW based on continuously tracking the menstrual cycle at the home of the woman. It is reasonable to assume that predicting the FW at the domestic environment, with less disturbance for the woman's life and routines as possible, will serve as a preferable solution for those who are interested in better identifying their FW not in the context of professional or medical settings with a highly automated system.

2. Methods

2.1. Study population

The study included 30 women at the age of 22-40, weight 61 (48-90Kg), BMI 22.1 (17.7-29.4). All participants were healthy, with regular menstrual cycle and no known ovulation or fertility issues. All participants signed a consent form, approved by the Herzliya Medical Center ethical committee, prior to the beginning of the study.

2.2. Protocol and data acquisition

Following the women's consent, the participants were provided with a piezoelectric sensor (EarlySense, LTD) to locate under their mattress, preferably under their sternum when lying on their bed, and an application to install on their private smartphone or tablet. If known, the participants were asked to fill-in their last menses' dates.

After the installation was completed, the system automatically tracked and recorded respiration and cardiovascular activity during night time in which the woman was in bed. The participants were also asked to document in the application their coming menses dates, once attained.

2.3. "Gold standard" reference and testing

In order to assess the ability of the algorithm to accurately predict ovulation time window, each of the participants was requested to come for 4-12 in-clinic visits during each of her menstrual cycles and take a medical examination which included the following tests:
- Transvaginal ultrasound which measure the growth of the egg follicles and the thickness of the uterine lining.
- Blood tests that measure the estrogen level in blood as additional indicator of the growth and maturation of the eggs.
- Appropriate blood tests to confirm pregnancy (if applicable).

The results of the above tests allowed the medical experts to determine ovulation dates. These dates were documented and used as "Gold standard" reference for offline comparison analyses.

2.4. Data analysis

The data analysis was conducted offline. For each of the nights of all participants, the system used the piezoelectric sensor data to compute the HR and RR throughout the night. In addition, the system ability to identify sleep stages allowed the extraction of HR and RR during the non-REM time intervals. Previously, a study that aimed to validate the system capability in measuring HR, RR, and sleep performance indicated for 96.1 % and 93.3 % accuracy rate for HR and RR, respectively, and in terms of sleep stages, an accuracy rate of 90.5 % [10]. In addition, a dedicated algorithm was developed to process and analyze, for each of the participants and for all of the menstrual cycles, the sensor data and the logged menses dates. The result of the algorithm was a prediction of in which dates the next FW should occur as well as the prediction of the next menses.

2.5. Accuracy testing

Analysis of accuracy was performed by measuring the overlap between the FW as detected by sensor technology to the FW as determined by the "Gold" reference method (i.e., expert physician decision based on results of the reference tests). FW was considered to be during the 5 days prior to the actual day of ovulation plus the day of ovulation for a total of 6 fertile days [1].
a 4 day overlap with the reference window, it was calculated that sensor is accurate by 66% for this specific ovulation cycle.

This analysis (sensor vs. "Gold" reference) was also compared to the accuracy of two additional common methods to predict ovulation day and fertility window as following:

Method 1: "Simple calendar estimate" is a common method used by physicians and includes an assumption that the duration of the luteal phase is 14 days for every woman. Hence, by subtracting 14 days from the presumed upcoming day of menstruation (based on women's reporting on their previous menses days), an estimation regarding the day of ovulation and accordingly the fertile window is made.

Method 2: "Multi month estimate" is achieved using the same method as method 1, with the difference of calculating the average duration of at least three menstrual cycles, and not relying only on the duration of one.

3. Results

3.1. FW prediction

Figure 1 presents the timeline of a. HR and b. RR throughout the menstrual cycle for all participants as were measured during non-REM sleep. Significant change was identified in the value of HR between the late follicular phase and the ovulation days (t(21)=2.61, p<0.01), stemmed from an increase in HR during the ovulation days. Also, the late follicular time period was characterized with a slow breathing rate (16.25 bpm) which was gradually increased throughout the luteal term and reached a value of 16.79 bpm (t(21)=1.94, p=0.05).

Figure 2 presents the average detection accuracy (overlap %) between the contactless sensor predicted FW vs. "Gold" reference, for each month. The accuracy of the "Simple calendar" and the "Multi-month" estimations methods relative to the "Gold" reference and in comparison, to sensor's detection capability is also presented.

Figure 3 shows an example of one parameter (nightly average respiratory rate) for one participant with 6 cycles. The vertical lines indicate the first reported menstrual day (red) and the ovulation day according to gold standard (black). The purple and the green squares indicate the predicted ovulation using "Multi month estimate" (purple) and the sensor’s data (green). As can be seen in the figure the ovulation is better predicted with the sensor’s measurement compared to the estimate based on past cycle length.

3.2. Menses prediction

Following the encouraging results of the FW prediction algorithm, an additional algorithm was developed, aiming to use the above collected sensor dataset and predict the dates of the coming menses. The preliminary results of the menses prediction algorithm indicate an ability to point on the next menses day in an accuracy error of 1.48 days.

4. Discussion

The aim of the current study was to examine whether a contact-less sensor that measures cardiovascular activity during the night can help to better predict the user's FW. Overall, the results indicate that the performance of the sensor and its dedicated algorithm outscored other accepted methods.

During the timeline of the menstrual cycle, different reproductive hormones are involved in synchronizing the fertilization process [11, 12, 6, 7]. The end of the follicular phase is characterized with a vast increase of LH to initiate and encourage ovulation. Progesterone and estrogen levels elevate after ovulation to support implantation and fall if fertilization did not occur. It is apparent that on top of their role in the reproductive system, they influence other systems as well, including the respiration and the cardiovascular systems. The progesterone increase during the luteal phase has an elevating effect on central noradrenaline release which in turn contributes to an increase in HR. The estrogen surge at the end of the follicular phase reduces RR. These lead to a large difference between the end of the follicular phase and the beginning of the luteal phase. This study's results indicate for a significant higher HR values during the ovulation and luteal phases, compared to the menses and the follicular phases [8]. Moreover, a relative low RR was found at the end of the follicular phase, which gradually increases up until the end of the luteal phase. Therefore, the results of the current study support the HR and RR oscillated trends. In addition, the results can be used as evidence for the ability of the contactless sensor to accurately measure HR, RR throughout the menstrual cycle.

For many of those who want to conceive, recognizing the FW is essential. However, this appears to be a challenging concern [1]. Previous works disagree on what is the number of fertile days within the menstrual cycle and it varies between 2 [13] up to 13 [14], highly depended on the specific population and the measurement methods used. Calculating FW based on the time of the previous menses is a straight forward method. Nevertheless, it is based on a guess of what is the length of the current menstrual cycle and of that the length of the luteal phase is relatively stable and lasts 14 days ("Simple calendar estimate"). If the individual's menstrual cycle length is not constant, the average of the last few cycles should improve accuracy ("Multi month estimate"). The results presented in figure 2 indicate that both the "Simple calendar estimate" and the "Multi month estimate" yield up to 65% overlapping accuracy with the "Gold" reference. The
results of the current study’s algorithm outscored both conservative methods. Its accuracy rate started at 63.8 %, equal to the two other methods as they all shared the same information at this point, which is the woman's last menses date. However, an increase in accuracy rapidly occurred across time and reached the level of 72 % after 3 months.

It is important to note that the potential of the three methods to improve their accuracy as time goes by is different. The "Simple calendar estimate" depends on the last and only month. It assumes strict rules - the lengths of the luteal phase and the menstrual cycle. Therefore, its accuracy, as appears in Figure 2, is rather limited (65 %). The "Multi month estimate" relies on several menstrual cycles and therefore is considered to be more precise throughout time due to the fact that the two "Simple calendar estimate" assumptions are not stable and accurate for all women [15, 16]. However, according to the data presented in Figure 2, no significant advantage of the "Multi month estimate" on the "Simple calendar estimate" was found. In contrast to that, the current's study algorithm results did improve throughout the months. Figure 3 demonstrated this notion. In the presented example, both the current study's algorithm and the "Multi month estimate" performed relatively the same at the first two months. However, unlike the current study's predictions, an error evolved in the "Multi month estimate" method as months continued to pass.

5. Study limitations

The population of the current study comprised of women with a BMI lower than 30, with no known health problems, with regular menstrual cycle and no known ovulation or fertility issues. However, as the sensor was previously used and tested with obese individuals (up to 400 lb; unpublished data), no reduction in accuracy of HR and RR was noted and therefore no change in the algorithm accuracy is expected. In addition, the respiratory and cardiovascular systems are affected by many daily activities that should be taken into account such as illness, habits of sport, smoking, food intake, and even alcohol consumption. In fact, this was the reason for focusing in non-REM sleep time intervals only in the analysis. It could be assumed that once these behaviours are documented and take into consideration, the algorithm performance and the system's accuracy should improve.

6. Conclusions

The results of the current study suggests that the use of the piezoelectric sensor, enhances the ability to accurately predict the fertile window, compared to the "Gold" reference. The sensor's predictive capability was found to be superior to the two most common methods of estimation used based on historical menstruation cycles "Simple calendar" and "Multi month" estimations that are based on women's reporting on their previous menses days.

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Figure 1. Group mean median (blue line) and standard error (error bars) for a. HR and b. RR during non REM sleep, throughout the menstrual cycle for all participants.
Figure 2: average detection accuracy (overlap %) between the contactless sensor predicted fertility windows vs. "Gold" reference, for each month. The accuracy of the "Simple calendar" and the "Multi-month" estimation methods relative to the "Gold" reference and in comparison, to sensor’s detection capability is also presented.

Figure 3: An example of one parameter (average respiratory rate – blue line) during 6 cycles (vertical red lines) and 6 ovulations (vertical black lines). The purple and the green squares indicate the predicted ovulation using "Multi month estimate" (purple) and the sensor’s data (green).
References


Address for correspondence.
Liat Tsoref.
Jabotinsky 7, Ramat Gan, 52520 ISRAEL.
Liat.Tsoref@earlysense.com