Accurate prediction of the fertile window using PRIYA Fertility Sensor: Optimizing measurements of continuous core body temperature

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Abstract

Background: The number of women who are waiting longer before starting a family has been steadily increasing over the past few decades[1], with challenges such as age-related fertility decline and irregular menstrual cycles, as they attempt to identify the "fertile window".

Continuous recording of core body temperature allows the identification of patterns associated with temporal rhythms that correlate with the release of luteinizing hormone (LH), estrogen and progesterone. Prima-Temp has developed a self-inserted flexible vaginal ring (the PRIYA Ring) that records core body temperatures every 6 minutes and passively communicates to the PRIYA App which can be installed on a wide range of smartphones.

Methods: This study (PT-004) is designed to compare the fertile window predicted by the PRIYA Sensor (Prima-Temp, Boulder, CO) vs that achieved with a urine LH ovulation prediction kit. Successful temperature data transmission rates from the PRIYA Ring to the App on mobile devices were also evaluated. The study contains 2 cohorts: Group 1 will include up to 20 subjects and Group 2 will include up to 50 subjects.

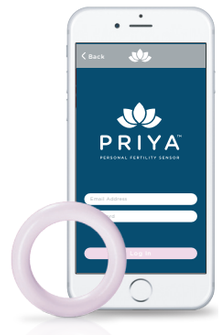
Results: A total of 16 subjects were enrolled in Group 1 to date. Fertility prediction data are currently available from the first evaluable cycles for 9 subjects. In all 9 cycles evaluated, the PRIYA Sensor predicted the fertile window an average of 2.3 days prior to the LH test. The most commonly reported adverse events, irrespective of a causal relationship to the device, consisted of mild abdominal cramps, vaginitis, and abdominal or pelvic pain. Virtually all adverse events were mild in severity and generally resolved without treatment within a few hours or days.

Conclusions: The PRIYA Sensor provides precise, continuous core body temperature measurement which is interpreted by a proprietary artificial intelligence algorithm to identify a woman's fertile window and wirelessly communicate this information to her smartphone. Early results with the PRIYA Sensor indicate that it is at least as effective as LH tests for predicting the fertile window and can reliably provide the fertile window predictions days ahead of the positive LH results. The PRIYA Sensor is safe and well-tolerated, and the ease of use may represent a significant advance in trying to conceive.

Introduction

- Despite recent advancements in fertility prediction, there are still a significant number of women and their partners who are trying to find an effortless yet accurate product to help them predict the 'fertile window'.[2,3]
- Many currently available products and tracking tools require a considerable amount of user interaction to record frequent temperature readings, urine test results, and other observations. This can lead to frequent errors, user stress, and frustration.[3-7]
- Basal body temperature (BBT) charting, urinary luteinizing hormone, salivary ferning and analysis, and external temperature reading have traditionally been used as aids for predicting ovulation.[3] However, the utility of these approaches is limited by:[8,9]
  - Cumbersome temperature measurement devices.
  - Vagaries of the charting process when left to the patient.
  - Lack of generally-accepted criteria for objectively interpreting BBT graphs; data is prospective and does not predict ovulation.
- Other fertility detection methods are unable to capture circadian rhythm patterns. These patterns provide reliable and consistent fertility indications for predicting ovulation[10,11] and is most reliable through 24/7 continuous core temperature monitoring.[11]
- The PRIYA Sensor (**Figure 1**) was developed to overcome the limitations of earlier BBT sensing and other fertility detection methods, and has the following characteristics:
  - Designed to predict and notify the user when core body temperature readings are consistent with 'the fertile window,' that is, the pre-ovulatory period of time most favorable for achieving pregnancy.
  - Thermometric device inside a flexible medical-grade silicone polymer continuously measures and records core body temperature (every 6 minutes), along with cycle length, to identify the most fertile phase of the menstrual cycle.
  - The sensor transmits core body temperature data wirelessly to a mobile device allowing the proprietary algorithm to predict the fertile window.
- The objectives of this study are to evaluate:
  - Successful temperature data transmission rates from the intravaginal PRIYA Ring to the PRIYA App on mobile devices.
  - Successful prediction of the fertile window vs LH testing.

Figure 1. The PRIYA Ring and PRIYA App



Methods

Study Design

- Open-label adaptive design study.
- Up to 20 participants are to be enrolled in the first group of the study and up to an additional 50 participants are to be enrolled in the second group to complete the trial.
- After signing an institutional review board-approved informed consent form, participants wear the intra-vaginal PRIYA Ring continuously during at least one menstrual cycle.
- Eligible participants assigned to 1 of 2 study groups:
  - Group 1: designed to assess recent software updates to the PRIYA App.
  - Group 2: designed to formally assess the usability, reliability, and accuracy of the PRIYA Sensor.
- After completion of the first menstrual cycle in either group, participants are given the option of continuing to wear the PRIYA Ring for up to 2 additional menstrual cycles.

Subjects: Key Inclusion and Exclusion Criteria

Inclusion

- 18 to 45 years of age.
- Body mass index (BMI) between 19 and 38 kg/m^2.
- Willing to use the PRIYA Sensor and complete study procedures according to protocol instructions.
- At least one normal Pap smear within the past 3 years, and if more than 1 test was performed, the most recent Pap smear result was be normal.
- Regular menstrual cycles (≤7 days difference between the shortest and longest cycle in the last 6 months, menstrual cycle ≥24 days and ≤35 days).
- Provided informed consent.

Exclusion

- Unresolved self-reported yeast infection, trichomonas, or bacterial vaginosis ≤14 days prior to screening.
- Known sensitivity or allergy to silicone or latex.
- History of hysterectomy, chronic pelvic pain, or pelvic inflammatory disease.
- Inability to tolerate a vaginal tampon, diaphragm, or similar type of intravaginal ring.
- Abnormal Pap smear result for the most recent test conducted within the past 3 years.
- History of vaginal or cervical cancer.
- Currently pregnant.
- Currently taking birth control pills or wearing an intrauterine device, NuvaRing®, or another intravaginal contraceptive ring.

Study Procedures for Cycle 1

- Within 3 days of baseline (first day of menstruation), subjects contacted the Principal Investigator to confirm and verify the PRIYA Sensor instructions for use.
- Subjects inserted the PRIYA Ring on the first day after the end of their periods and started twice daily testing (morning and evening) with an LH test kit and continued until a positive result (LH high) was detected followed by a negative result (LH low).
- Subjects also checked the temperature transmission data on the PRIYA App at least once a day and notified site personnel if they had any difficulty synchronizing the Ring and the App.
- At the end of Cycle 1 (within 3 days after the first day of the next period), the subject contacted the Principal Investigator to complete a follow-up assessment for Cycle 1 that included:
  - Adverse events, including pain or discomfort with the use of the PRIYA Ring.
  - Unanticipated problems with the PRIYA Sensor.
  - Changes in use of over-the-counter or prescription medications.

Methods (cont.)

Data Analysis

Study Populations

- Modified Intent-to-treat (mITT): eligible subjects assigned to receive the PRIYA Ring and mobile devices who at least attempted to pair the devices and wear the PRIYA Ring for Cycle 1.
- Per protocol: members of the mITT population who complied with all study-related procedures, including wearing the PRIYA Ring for at least 1 cycle and performing twice daily LH tests (morning and evening) on the days stipulated.

Data Analysis

- The number and percentage of subjects completing successful transmissions of temperature data will be summarized.
- Based on the refined algorithm developed on the temperature data collected over the course of the study, correlations between positive LH test results and PRIYA App ovulation predictions will be summarized.
- The number of days prior to the positive LH test result that the PRIYA Sensor predicted ovulation was also calculated and summarized.

Preliminary Results

Participants

- To date, 16 participants were enrolled into Group 1 and 12 completed ≥1 cycle.
- Two participants discontinued due to adverse events and 2 withdrew consent prior using the PRIYA Sensor.
- Nine participants provided a total of 17 evaluable cycles. An evaluable cycle is defined as at least 4 days of temperatures before the LH-high and no time gaps (ring removed or no readings) of more than 3 hours before the LH-high.
- The demographic characteristics for the overall population and for subjects with evaluable cycles are summarized in **Table 1**. Data for the first cycles for 9 women are provided in this preliminary analysis.

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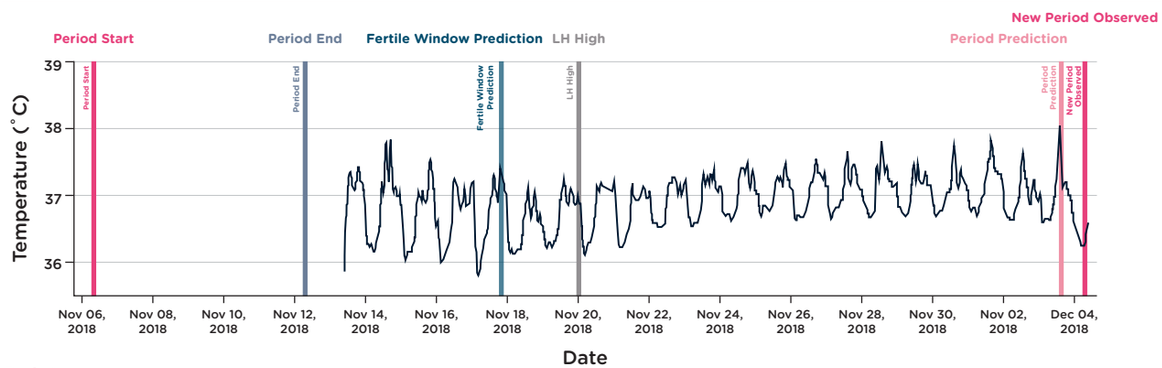
Table 1. Demographic Characteristics of Group 1 Subjects

	Overall Group 1 Population to Date (N =16)	Group 1 Subjects with Evaluable First Cycles (N = 9)
Age (years):		
Mean	34.4	34.2
Median	34.8	34.5
Minimum, Maximum	25.0, 45.6	27.0, 40.6
Standard Deviation	5.74	4.44
Race/Ethnicity:		
White	15	9
Black or African American	0	0
Asian	0	0
Other	1	0
Hispanic	0	0
Non-Hispanic	16	9
BMI (kg/m²):		
Mean	22.5	22.7
Median	22.1	22.3
Minimum, Maximum	17.9, 30.0	19.4, 29.1
Standard Deviation	3.42	3.20

Efficacy

- Efficacy results are presented for the first evaluable cycle for each of the 9 subjects in this analysis.
- Temperature data was successfully transmitted from the PRIYA Ring to the App on mobile devices for all evaluable subjects.
- In this preliminary analysis, the PRIYA Sensor predicted the fertile window an average of 2.3 days prior to the LH test (SD 1.4 days) (**Figure 2**).

Figure 2. Temperature Recordings from One Subject



Safety

- The most commonly reported adverse events, irrespective of a causal relationship to the device, consisted of mild abdominal cramps, vaginitis, and abdominal or pelvic pain.
- Virtually all adverse events were mild in severity and generally resolved without treatment within a few hours or days.

Conclusions

- The PRIYA Sensor predicted the fertile window an average of 2.3 days prior to the LH test. The PRIYA Ring was safe and well-tolerated. Virtually all adverse events were mild in severity and generally resolved without treatment within a few hours or days.
- Measurement of core body temperature with the PRIYA Sensor overcomes important limitations of LH urine assay and other approaches for prediction of ovulation:
  - Requirement for user interaction and data recording that may result in significant errors[3-7] is eliminated by automated data collection and delivery to the PRIYA App.
  - The PRIYA Sensor is simple to use vs conventional cumbersome devices.[8,9]
  - The PRIYA Ring can be left in place, and all measurements are taken and recorded automatically. There is no need for high adherence to strict measurement and recording requirements.[12]
  - The accuracy shown for the PRIYA Sensor in predicting the fertile window may eliminate the need for urine testing, to avoid confounding factors that complicate the use of LH testing.[13]
- In summary, the PRIYA Sensor provides precise, continuous core body temperature measurement which is interpreted by a proprietary artificial intelligence algorithm to identify the fertile window and wirelessly communicate this information to a smart phone. Data for Groups 1 and 2 will be reported soon to confirm these preliminary findings.

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