**Study Protocol**

Study Title: Investigating the utility of a fetal motion sensor in measuring fetal movements

Short Title: Fetal Kicks

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**1. INTRODUCTION**

The following study will be a comparative study for patients utilising a novel fetal movements sensor, Fetal Kicks, to objectively measure fetal movements in comparison to available measurement modalities. The following study aims to function as an observational study for the current generation of Fetal Kicks (v3.0) in:

* Accurately detect fetal movements and filter out maternal activities.
* Performing overnight, up to 12 hours.

This will be achieved by collecting signals generated during maternal activities to update and train the machine learning algorithm to automatically differentiate fetal movements and maternal activities. Besides, the performance of the device over an extended duration will also be studied by trialling the Fetal Kicks device on pregnant mothers for up to 12 hours.

**2. BACKGROUND**

Fetal movements are described as a discrete kick, flutter, swish or roll and are indicative of the integrity of a well-functioning central nervous system and musculoskeletal system [1].

It is estimated that reduced fetal movements (RFM) occur in up to 15% of pregnancies [2]. When a fetus is compromised in utero, it decreases its movements in an effort to conserve oxygen and which is considered a predecessor to in utero fetal death or stillbirth [3]. At present, however, there is disparity internationally in terms of the definition for what constitutes as RFM - due to the paucity of robust epidemiological studies on patterns of fetal activity as well as the maternal perception of these movements [4, 5]. Also, the level of movement which distinguishes a healthy fetus from one which is compromised is yet to be determined as well [6].

One contributing factor to this is the lack of a robust manner to measure the movements of the fetus [7]. Its measurement, at present, is largely subjective, requiring a mother to report movements experienced, termed formal fetal counting (FFM). For FFM, there are several methods which stipulate various time periods over which mothers may count and report their movements. A systematic review however, failed to demonstrate any benefit in reducing fetal morbidity and mortality through this manner of self-assessment [8]. Furthermore, fetal movements can occur in up to 40% of cases without the mother realising it [8]. Objective manners of assessment include the use of real time ultrasound to detect movements as well. Although slightly more sensitive then FFM in terms of detecting fetal movements (31.4%- 57.2% vs 30.8 %), there are several technical shortcomings associated with the technology which include the mother having to lie to in a semi recumbent position for 20 to 30 minutes and the detection of false positive ‘movements’ (from the transducer compression of the abdominal wall and coughing etc) as well [9].

The presence of RFM has been associated with an increased risk of adverse perinatal outcomes, related to fetal growth restriction, as well as still birth [3]. In addition, there is evidence to demonstrate that increased surveillance will allow for induction of high-risk women which will reduce the stillbirth rate as well in these pregnancies as well- providing an intervention to utilise should an abnormality be detected [10]. Given this association, one may question why there is a lack of robust evidence to guide what is normal fetal movement patterns and maternal perception of these.

In addressing these current shortcomings, Fetal Kicks device has been innovated with the intention of providing a more objective manner of assessing these movements. Fetal Kicks device will be worn abdominally as a patch and will utilise surface sensors to detect fetal movements. This study therefore, aims to investigate the validity and reproducibility of Fetal Kicks device in signal acquisition and detecting fetal movements.

To achieve this, our current phase of study encompasses testing ability of the Fetal Kicks device in differentiating maternal activities and fetal movements, as well as the ability to perform over an extended period up to 12 hours.

The midwife at the Royal North Shore Hospital in St Leonards will scan the participant’s abdomen under ultrasound in semi recumbent position for up to 10 minutes. During this period, the sonographer will identify the position of the baby.

After that, the participant will be taught by the study coordinator or midwives to attach the soft Fetal Kicks device(s) on her belly and activate the data recording process. The study coordinator will also install the app on the participant’s smartphone device, and a log file will be generated on her phone which will be extracted by the study coordinator upon completion of the trial.

The soft Fetal Kicks device(s) will be attached on the belly by the participant at home, 30 minutess before bed. After that, the participant will be required to perform activities below:

1. Lifting up an object for 10 times
2. Twisting body left and right for 10 times each
3. Bending down for 10 times
4. Standing for 5 minutes
5. Walking for 5 minutes
6. Lying down for 5 minutes
7. Sitting for 5 minutes

Following this, the participant will be required to continue wearing the device until the next morning when she’s awake. The participant can remove the soft Fetal Kicks device(s) when she’s awake. The device(s) are not waterproofed so they should not be worn during shower.

At the conclusion of this study, the participant will have to return the device(s) to the study coordinator / midwifes, and a form will be given to her to evaluate her experience with the study process and to provide feedback on the device as well as the aspects which could be improved upon and raise any safety concerns she might have had during the monitoring process.

The data of Fetal Kicks device and accelerometer will be compared and the machine learning algorithm will be updated and trained to differentiate the maternal movements and fetal movements.

Once the proof-of-concept stage has been completed and the device efficacy has been assessed, we may have a more reliable manner of studying fetal movements. This in turn can be utilised to conduct larger population-based studies to establish a range for normal fetal movements and further contribute to the delineation of a definition for RFM.

**3. AIM(S) AND OBJECTIVES OF STUDY**

The aims and objectives of the following study is to function as a proof-of-concept study for Fetal Kicks device in:

* Accurately detect fetal movements and filter out maternal activities.
* Performing over an extended duration of up to 12 hours.

**4. HYPOTHESIS**

**Primary Hypothesis**

H0: Fetal Kicks device is able to differentiate fetal movement and maternal activities.

HA: Fetal Kicks device is not able to differentiate fetal movement and maternal activities.

**Secondary Hypothesis**

H0: Fetal Kicks device is able to perform over extended period of up to 12 hours

HA: Fetal Kicks device is not able to perform over extended period of up to 12 hours

**5. STUDY DESIGN**

The following study is a cross sectional survey with a cohort design and is the design of choice in evaluating a diagnostic test such as Fetal Kicks [11]. Utilising the following design, measurements of test accuracy, reliability and precision will be carried out on Fetal Kicks in over extended period of up to 12 hours.

**6. STUDY SETTING/LOCATION**

The following study will be carried out at Royal North Shore Hospital Monash Health Pregnancy Assessment Unit. The following study is a multi-site study.

**8. STUDY POPULATION**

The study population will be obtained from women presenting to the Pregnancy Assessment Unit for evaluation of Fetal Kicks. Inpatient women from the maternity wards, maternity clinic, and perinatal care centre will also be enrolled in this study. For the analysis, 100 women will be recruited via convenience sampling.

**9. ELIGIBILITY CRITERIA**

**Inclusion criteria**

The women in the following group:

1. Have a singleton pregnancy
2. Should be pregnant and above 28 weeks of pregnancy
3. Should be aware of what normal fetal movements are
4. No presentation for reduced fetal movements during the current pregnancy
5. No congenital abnormality in the fetus

The following criteria are relevant as:

1. Multiple order pregnancy will complicate data interpretation at a proof-of-concept level
2. In the primigravida, some women may not be aware of what normal fetal movements are and this perception has to be validated which is generally above 16 weeks of gestation
3. There is no literature to accurately guide what normal fetal movements entail and at present an individualised approach of considering maternal perception of reduction is utilised to consider a clinically significant reduction in movement.

**Exclusion criteria**

1. Women below 18 years of age
2. Patients with an intellectual or mental impairment
3. People in existing dependent or unequal relationships with any member of the research team, the researcher(s) and/or the person undertaking the recruitment/consent process
4. People highly dependent on medical care

**10. STUDY OUTCOMES**

**Primary Outcome**

The primary outcomes for the following study will include:

1. Preliminary validation of Fetal Kicks device’s reliability and ability of device to filter out maternal activities
2. Determination of optimal Fetal Kicks device locations maternal abdomen
3. Improved reliability of Fetal Kicks device through inclusion of pregnant sources of noise
4. Validation that the Fetal Kicks device can detect FM.
5. Validation that the Fetal Kicks device can perform reliably for an extended period.

**Secondary Outcome**

1. Patient feedback on Fetal Kicks device

**10. STUDY PROCEDURES**

**a. Participant recruitment**

For the following study, participants will be recruited via convenience sampling from women presenting at the Pregnancy Assessment Unit, Fetal Surveillance unit, and inpatient wards at Monash Medical Centre and Royal North Shore Hospital based on the inclusion criteria. To establish potential candidates to approach, the bookings for day assessment patients will be reviewed daily as well to earmark potential candidates for participation in the trial.

**b. Randomisation and Blinding**

For the following study, during data collection, patients will be blinded to the smartphone screen. No randomisation of participants will be carried out.

During data analysis, given the way the results are to be analysed and interpreted, one cannot blind the investigators during the analysis of the results as well.

**c. Study procedures**

Prior to the monitoring, the women will be asked a few questions to obtain their demographic data and pregnancy related information. This will include a measure of their height and weight as well, which is a routine aspect of antenatal care.

This study is designed to run for up to 12 hour per session at the Royal North Shore Hospital in St Leonards, New South Wales and Monash Health at Clayton, Victoria.

The midwife at the Royal North Shore Hospital in St Leonards will scan the participant’s abdomen under ultrasound in semi recumbent position for up to 10 minutes. During this period, the sonographer will identify the position of the baby.

After that, the participant will be taught by the study coordinator or midwives to attach the soft Fetal Kicks device(s) on her belly and activate the data recording process. The study coordinator will also install the app on the participant’s smartphone device, and a log file will be generated on her phone which will be extracted by the study coordinator upon completion of the trial.

The soft Fetal Kicks device(s) will be attached on the belly by the participant at home, preferably at late evening before bed. After that, the participant will be required to perform activities below:

1. Lifting up an object for 10 times
2. Twisting body left and right for 10 times each
3. Bending down for 10 times
4. Standing for 5 minutes
5. Walking for 5 minutes
6. Lying down for 5 minutes
7. Sitting for 5 minutes

Following this, the participant will be required to continue wearing the device until the next morning when she’s awake. The participant can remove the soft Fetal Kicks device(s) when she’s awake. The device(s) are not waterproofed so they should not be worn during shower.

At the conclusion of this study, the participant will have to return the device(s) to the study coordinator / midwifes, and a form will be given to her to evaluate her experience with the study process and to provide feedback on the device as well as the aspects which could be improved upon and raise any safety concerns she might have had during the monitoring process.

For data analysis, CI Marzbanrad will extract data from of 1) Fetal Kicks device detected movements based on dynamic signal criteria, 2) sonographer timestamp, 3) maternal timestamps and 4) accelerometry data to generate fetal movement profiles based on signal processing techniques. This will allow for digital comparison of the various timestamps to assess reliability. The investigators will consider agreement between maternal perception and perceived movements if they occur between 2 seconds of each other. Movements < 2s apart were considered to be the same movement. Maternal perception < 2s apart were considered to be the same episode of maternal perception. A fetal movement was considered perceived (by maternal perception or Fetal Kicks device) if it was within 2s of an ultrasound movement being visualised

For each of the stages, all patient output data will be linked to a single numerical identifier which will be utilised from that point for analysis by the researchers. Data obtained will be securely stored on file on a secure hard disk drive and subsequently uploaded to a cloud server with HIPAA based security.

There is no follow up expected of you after completion of this initial stage of monitoring.

Following monitoring, your information will be stored which will allow us to contact you in the unlikely event that an adverse side effect from the device is discovered.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

**d. Measurement tools utilised**

In assessing the primary outcomes:

Measurements will be done electronically on Fetal Kicks device, using timestamp integration and the accelerometry patch.

In assessing the secondary outcomes:

To assess the secondary outcomes, the demographic data of the patients will be collected at the time of consent. This information will be obtained from questionnaires administered at the time of consent.

**e. Safety considerations/ Patient safety**

For the following device, the technology being utilised is conventional and has previously been utilised safely in pregnant individuals (Phase A of study) with no adverse reports in pregnancy (refer to attached Investigator brochure).

In monitoring the adverse effects associated with utilising Fetal Kicks device, the patient information sheet will have the contact of the trial coordinator who they can contact if they experience any safety issues or concerns regarding how the data collection process had been carried out. This information will be returned to the research supervisors who will address the concerns in direct consultation with the patient or advise suitable recourse if the issue is deemed to be under the purview of Monash Health and Royal North Shore Hospital directly.

If during the trial, any incidental findings of clinical relevance are noted, these shall be reported to the study doctor who will report these to the patient’s treating team. In the event of an emergency incidental finding, the study researchers will alert the clinical staff and report this to the study doctor.

**11. STATISTICAL CONSIDERATIONS AND DATA ANALYSIS**

**11a. Sample size and statistical power**

For the following study, a sample size of 100 is considered sufficient, based on expert opinion, to create a working data set which can compare device efficacy and simultaneously be analysed using machine learning techniques to subsequently function as a standalone algorithm to identify fetal movements autonomously.

**11b.** **Statistical methods**

For this study, demographic data will be expressed using summary statistics utilising parametric procedures.

Intraclass correlation coefficients and Bland Altman analysis will be undertaken to assess reliability. Receiver operating characteristic curves will be generated to Machine learning techniques will also be utilised in an attempt to classify.

Qualitative methods will be utilised to analyse patient feedback on the device.

**12. ETHICAL CONSIDERATIONS**

The study will be conducted in full conformance with principles of the “Declaration of Helsinki”, Good Clinical Practice (GCP) and within the laws and regulations of Australia.

A detailed overview of the ethical considerations is detailed in the attached National Ethics Application Form

**13. OUTCOMES AND SIGNIFICANCE**

Through conducting the following study, we hope to be able to achieve the objective of investigating the efficacy of Fetal Kicks device in monitoring fetal movements trans abdominally accurately in comparison to the subjective methods employed at present.

The benefits of conducting the following study will be:

 Developing a tool which may help monitor fetal movements accurately which is an aspect in pregnancy care which is still lacking

 Providing 24/7 fetal surveillance in pregnancies for fetal movements

 Acting as a surrogate surveillance tool for stillbirth

Should the monitoring potential of Fetal Kicks device be established, this will pave the path for testing the device in alternative scenarios such well – such as in normal pregnancies to get a better understanding of normal fetal movement patterns as well.

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