Study Protocol Title:

Elevation of the Fetal Buttocks Prior to External Cephalic Version

Study Sponsor:
AdventHealth Orlando

Principal Investigator:
Principal investigator: D. Ashley Hill, MD.

NCT04538261

IRB Approval Date:
11/23/2021

List of Abbreviations:

ECV	External Cephalic Version
FHR	Fetal heart rate
FDA	Food and Drug Administration
VAS	Visual Analog Scale
EMR	Electronic medical record

Introduction

This document is a protocol for a human research study. This study will be conducted in accordance with applicable federal regulations and institutional research policies and procedures.

Background Information and Scientific Rationale

Breech presentation, where the baby's buttocks or feet are presenting first, occurs in 3-4% of pregnancies after 37 weeks gestational age.[1] Options for patient with a term breech baby include cesarean delivery, attempted vaginal breech delivery, or attempted conversion from breech to a head first (cephalic) presentation using a procedure called external cephalic version (ECV). Breech vaginal deliveries are increasingly less common due to findings from a meta-analysis and systematic review that a planned cesarean delivery reduced both perinatal and neonatal death.

Many patients would like the opportunity to deliver vaginally, and in most cases those patients with a breech presentation after 36 weeks gestational age may be offered an ECV. ECV has varying rates of success depending on many factors, including whether the woman has had any prior pregnancies, the position of the baby, the amount of amniotic fluid, and whether the buttocks are deeply engaged in the pelvis.

Many obstetricians prefer to attempt ECV between 36-37 weeks gestational age because the success rate is similar to 34 weeks, but the baby is less likely to need neonatal intensive care if an emergent cesarean delivery is necessary. The success rate for nulliparous patients (those who have never delivered before) without spinal or epidural anesthesia is approximately 30%.

There are very few interventions to improve the success of ECV. A randomized trial of nulliparous patients undergoing ECV with and without spinal anesthesia found a success rate of 32% without and 67% with anesthesia. While this is an impressive improvement in success, many of our patients do not wish to have regional anesthesia. Regional anesthesia also increases the length of stay and cost of the ECV procedure. One potential method of improving ECV success is to elevate the fetal buttocks during the procedure, although this has been poorly studied. One group reported that they had zero successful ECV procedures when the buttocks were lower than -1 station, versus a 66% success if the buttocks were at or higher than -3 station.

The Safe Obstetric Systems Inc. Fetal Pillow is a balloon device approved by the United States Food and Drug Administration (FDA) for elevating the fetal head during cesarean deliveries performed during the 2nd stage, after the patient has been pushing. The device is placed into the vagina, filled with sterile saline, and inflated to push the head up and out of the pelvis. Using the device to elevate the fetal buttocks prior to an ECV is an off-label usage of the product. Although unlikely, it is possible that the Fetal Pillow may decrease ECV success rates or cause unforeseen harm to the mother or fetus.

The objective of this research project is to assess the efficacy of the Fetal Pillow during ECV procedures for nulliparous women without regional anesthesia.

Study Objectives

Primary Objective

The primary objective of this study is to evaluate the successful conversion of a breech to vertex presentation. Successful conversion will be confirmed via ultrasound immediately following the ECV procedure.

Secondary Outcomes

Maternal outcomes:

1. MRN
2. Age
3. Weight
4. Height
5. Body mass index
6. Ethnicity
7. Gravidity (total number of pregnancies including this one)
8. Parity (births > 20 weeks)
9. Number of vaginal deliveries
10. Number of cesarean deliveries
11. Measurement of inferior aspect of rib to pubic symphysis
12. Date and time of delivery
13. Induction
14. Presence of vaginal delivery (SVD or OVD)
15. Presence of vacuum assisted delivery
16. Presence of forceps assisted delivery
17. Presence of cesarean delivery
18. Fetal presentation at time of delivery
19. Presence of postpartum hemorrhage (> 1,000 mL of measured blood loss)
20. Presence of placental abruption
21. Presence of shoulder dystocia
22. Date and time of discharge after delivery
23. Length of stay
24. Cost of hospital stay (labor and delivery)
25. Patient zip code
26. Patient insurance

Neonatal outcomes:

1. Presence of stillbirth
    a. If stillbirth, estimated gestational age this occurred (weeks and days)
2. Birthweight (grams)
3. Apgar score at 1 minute
4. Apgar score at 5 minutes

5. Presence of neonatal intensive care unit admission
6. Presence of intubation
7. Presence of neonatal humeral fracture
8. Presence of neonatal clavicle fracture
9. Presence of neonatal skull fracture
10. Neonatal length of stay
11. Cost of neonatal stay

Procedural Outcomes

1. Date of procedure
2. Time of procedure
3. EGA
4. Name of obstetrician performing ECV procedure
5. Presence of inflated Fetal Pillow
6. Presence of terbutaline
7. Presence of palpable fetal head
8. Estimated fetal weight (kg)
9. Fetal head position *confirmed by ultrasound
10. Fetal back position
11. Position of fetal neck
12. Location of placenta
13. Amniotic fluid index (4 quadrant total)
14. Fetal station (-3 through +3)
15. Maternal cervical dilation (cm)
16. Presence of rupture of membranes within 1 hour of procedure
17. Presence of 3 or more contractions in 10 minutes immediately prior to procedure
18. Bleeding equal to a menstrual period during or within 1 hour of the ECV procedure.
19. Development of a pelvic hematoma during or within 1 hour after the ECV procedure.
20. Development of a vaginal laceration during insertion of the device, the ECV procedure, or removal of the device.
21. Presence of fetal bradycardia
22. Presence of fetal heart rate decelerations
23. Presence of delivery within 1 hour of procedure
24. VAS pain score immediately prior to ECV (-3 minutes)
25. VAS pain score immediately after insertion of Fetal Pillow (+ 2 minutes)
26. VAS pain score after inflation/sham inflation (+ 1 minute)
27. VAS pain score immediately after each ECV procedure attempt, maximum of 4 attempts (+ 2 minutes)
28. Total number of attempts
29. Procedure successful Y N (Primary Outcome) *confirmed by ultrasound
30. Fetal head position post ECV *confirmed by ultrasound
31. Number of forward rolls
32. Number of reverse rolls
33. Note which procedure was successful

34. Did patient request to have spinal or epidural anesthesia after initiation of ECV procedure (off of study protocol): Y N
35. Presence of regional anesthesia prior to ECV procedure (Excluded from study)
36. Length of time from start of procedure to hospital discharge
37. Cost of hospital stay for ECV procedure

Study Design

Research Design

This is a prospective, randomized double-blind clinical trial evaluating the effect of a balloon device to elevate the fetal buttocks during external cephalic version procedures. Eligible study population: pregnant women between 37-40 weeks estimated gestational age with a breech presenting baby and no contraindications to ECV.

Study Agent, Device, and/or Intervention Description:

The Safe Obstetric Systems Inc. Fetal Pillow is a sterile balloon device that comes in a sterile, single-use package (please see attached information). The Food and Drug Administration (FDA) has reviewed this device and determined it to be Non-Significant risk (NSR) because it does not meet the definition of a significant risk (SR) device under 21 CFR 812.3(m) of the investigational device exemptions (IDE) regulation (21 CFR 812).The device will be provided at no charge to AdventHealth Orlando. Drs. Hill or Lense will place the pillow into the vagina then the pillow will either be inflated/sham inflated by the midwife/physician with sterile saline in order to raise the fetal presenting part. After the procedure the device is deflated, removed and discarded. The Fetal Pillow device will be stored in a climate-controlled, locked storage area in the women's hospital accessible to the study investigators, midwife/physician and research personnel. It is possible that the manufacturer of this device may report de-identified study data to the FDA at a later date.

Study Site/Location and Number of Subjects

- AdventHealth Orlando.
- Estimated number of subjects: 138

Multi-Site Research Logistics/Communication Plan: N/A

Research Conducted in a Foreign Country: N/A

Community-Based Participatory Research: N/A

Subject Selection

Vulnerable Populations:

While the study population consists solely of pregnant women (some of whom may be AdventHealth Orlando employees), this research is unlikely to present more than minimal risk to subjects. This device has been used successfully to elevate the fetal head during difficult cesarean deliveries, and is FDA approved for this indication. If the device functions similarly to elevate the fetal buttocks, it may improve the success rate for the external cephalic version procedure, thus decreasing the risk that pregnant women may need a cesarean delivery. Because this research involves a procedure unique to pregnancy, it requires consent from pregnant patients. Patients unable to understand the consent process are excluded.

Inclusion Criteria

1. Breech presenting part as diagnosed by bedside sonography.

2. Pregnancy is between 37-40 weeks gestational age.
3. Live fetus.
4. Patient is >/= age 18.
5. Patient speaks English or Spanish as primary language.
6. Patient able to understand verbal and written consent

Exclusion Criteria

1. Non-breech presentation (cephalic, transverse, oblique).
2. More than 1 fetus.
3. Cervical dilation of >/= 1cm.
4. Prior uterine incision.
5. Congenital uterine anomaly.
6. Body mass index more than 40 kg/m^2.
7. Uterine fibroids causing soft tissue dystocia.
8. Extended fetal neck.
9. Oligohydramnios (4-quadrant amniotic fluid index </= 5cm).
10. Spontaneous rupture of membranes.
11. Any contraindication to vaginal delivery (ie placenta previa, placental abruption, active genital herpes outbreak).
12. Intrauterine growth restriction (estimated fetal weight </= 10%ile).
13. Estimated fetal weight > /= 5,000 grams for non-diabetic patient or >/= 4,500 grams for patient with pre-existing or gestational diabetes, confirmed by ultrasound.
14. Fetal gastroschisis.
15. Fetal neural tube defect.
16. Severe-range preeclampsia.
17. Patient had regional anesthesia immediately prior to ECV.

Resources Available

Team members have been involved in the development of the study protocol and analytic plan. Dr. Hill is the chair of the obstetrics and gynecology department of the AdventHealth Orlando Graduate Medical Education program, has authored numerous peer-reviewed publications and is an expert reviewer for several journals. Dr. Lense is the medical director of the AdventHealth Orlando Obstetric Specialists team and has authored several medical journal articles. An honest broker working in the department of Advent Health Children and Women Clinical Analytics.

Study Procedures

Subject Recruitment and Screening: Researchers will mail, fax and email an informational sheet describing the study, list inclusion and exclusion criteria, and provide contact information for obstetric providers to contact the researchers to discuss whether their patient qualifies for study inclusion.

If eligible, either Dr. Hill or Lense will contact the patient to discuss study participation, answer questions, and schedule the procedure, in coordination with the labor unit scheduling staff.

Consent Process: Potential research subjects will be screened for inclusion and exclusion criteria and scheduled for their ECV procedure. Dr. Hill or Dr. Lense will review the ECV procedure with the subject including the potential risks versus benefits of the Fetal Pillow device. Subjects will also receive written information at the hospital and will sign an informed consent document (HRP 500). At this time subjects will receive a screening number, which will be obtained from the master subject list. Researchers will follow HRP-802 and HRP-803 for guidance when obtaining informed consent. (Declining participation will not impact patient care: patients who do not consent to participate but who also want an ECV procedure will undergo an attempted ECV outside of the study protocol).

Documentation of Informed Consent Process

Documentation of the informed consent process is required to establish that the subject was accurately and adequately informed and that no study-related procedures were initiated prior to obtaining informed consent. A research team member will note in the source documentation the consent process, date and time consent was obtained and that consent was obtained prior to initiating any research procedures.

Non-English Speaking Subjects:

Dr. Lense is fluent in Spanish and will consent patients verbally (Spanish) and in writing (consent form written in Spanish).

Subjects who are not yet adults (individuals under the age of 18): N/A

Cognitively Impaired Adults: N/A

Adults Unable to Consent: N/A

Waiver of Consent: N/A

Randomization:
Patients will be randomized 1:1 using a block scheme using statistical software. Randomization assignments will be sealed into sequentially numbered, opaque envelopes which are stored in the locked study cabinet on the labor and delivery unit. A trained unblinded practitioner will obtain the randomization envelope from the locked study cabinet and will note the randomization number on the randomization form. The subject master list will be kept electronically in the Teams files only accessible by Drs. Hill, Lense and the research personnel. Only Drs. Hill, Lense, trained midwives/physicians and research coordinators will have access to the locked study cabinet.

Study Visits:

Visit 1 (ECV Procedure): The PI/Sub-I will meet the patient at the labor and delivery area, and review both the ECV procedure and possible study inclusion. The patient and researcher will sign consent forms if the patient qualifies for study inclusion and agrees to participate.

After weighing the patient, calculating a body mass index, performing a digital cervical exam, and performing a fetal non-stress test and obstetric ultrasound, all routine components of the ECV process, the PI/Sub-I will verify there are no exclusion criteria. Assuming that an ECV is still necessary and safe, the patient will receive a 0.25mg subcutaneous injection of terbutaline, a medication to quiet the uterus that is commonly used for ECV procedures. The midwife/physician performing the device inflation or sham inflation will open the randomization envelope. The researchers are blinded to patient randomization. All patients will mark a line on a 100mm VAS to assess pre-procedure pain.

The researcher will show the patient the device, open the sterile container, and insert the device into the vagina per manufacturer's guidelines for all patients in the study. All patients will mark a line on a 100mm VAS to assess post-insertion pain. The study physician will then obtain the assistance of a trained midwife/physician to inflate the device or perform a sham inflation. For the physician to remain blinded, the physician will leave the room during the time of the inflation/sham inflation. This will be documented in the source documents. Midwives/Physicians performing the inflation or sham inflation will have undergone previous training. Inflating the

Fetal Pillow is similar, although less difficult, than other balloon devices commonly used on the labor and delivery unit. The assisting midwife/physician will inflate the device with180 mL of saline for those patients randomized to inflation. This will occur under a sheet so that the patient is blinded to the randomization scheme. If the patient is randomized to no inflation, the midwife/physician will perform a sham inflation, also under a sheet. All patients will mark a line on a 100mm VAS to assess post-inflation/sham inflation pain. The assisting midwife/physician then leaves the room, and the study physician reenters the room and proceeds with the ECV procedure.

Regardless of randomization, at this point the ECV procedure proceeds using normal routine. Once completed, all patients will mark a line on a 100mm VAS to assess post-ECV pain. The ECV will be attempted up to four times and VAS will be assessed after each attempt.

The research physician will then remove the Fetal Pillow and perform a post procedural ultrasound to verify fetal position. Regardless of randomization, the procedure is completed per the usual routine of fetal monitoring, assessing for labor or bleeding, discussing post-procedure care, then discharge home (or, less likely, admitting for either observation or delivery).

The researcher will fill out the ECV portion of the data collection form.

Visit 2 (Labor and Delivery): There are no study interventions during this visit. The file linking the subject's FIN and study numbers will be sent to the honest broker who will then extract the data for delivery outcomes for the mother and neonate along with the final cost calculations This data will be entered into a spreadsheet by the honest broker and then sent back to the research team. The research team will send the file linking the subject's FIN and study numbers at the intervals outlined in the safety monitoring plan (first 10 randomized subjects and every 20 subjects thereafter). The investigators are unblinded to patient randomization after the ECV procedure has been completed and during data collection for delivery and neonatal outcomes.

Data collection for patients delivering outside of AdventHealth facility. Patients will sign a release of records; study coordinator will request records from delivering facility and delivery outcomes data will be imported into spreadsheet linked to FIN.

Study Duration:

Estimated date of study completion: March 31, 2023

- Projected start date: November1, 2020.
- Projected completion of enrollment of all study subjects: November1, 2022.
- Projected final data collection date: March 1, 2023.

Materials of Human Origin: N/A

Study Outcome Measures (Endpoints)

Primary Outcome:

Proportion of patients undergoing ECV who have a successful outcome with and without an inflated Fetal Pillow.

Secondary Outcomes:

As noted, many of these data points are normally recorded in the medical record during an ECV procedure and subsequent delivery, regardless of study participation.

Subject Information (maternal):
Demographic information of the patient will be collected in the electronic medical record (EMR) by noting ethnicity, number and type of prior deliveries, and measuring height and weight.

Subject Information (neonatal):

Neonatal gestational age at delivery, weight, 1 and 5 minute Apgar scores will be recorded from the medical record..

Pain perception:
Patients will complete a VAS pain scale prior to and after the ECV procedure as well as after the insertion of the fetal pillow and after the inflation/sham inflation of the pillow.

Impact of maternal parameters on successful ECV:
Researchers will measure the distance from the inferior aspect of the ribs to the pubic symphysis using a tape measure, location of placenta by performing an obstetric sonogram, and cervical dilation by performing a digital cervical examination.

Impact of fetal parameters on successful ECV:
A digital vaginal examination will determine the location of the fetal buttocks in the pelvis. The fetal head will be assessed to determine if it can be palpated on abdominal exam. The physician will perform an obstetric ultrasound and measure estimated fetal weight, amniotic fluid index, and position of the fetal neck.

Outcome of ECV procedure: Researchers will document the fetal heart rate pattern, and whether bleeding, contractions, labor, or rupture of membranes occur. If rupture of membranes is suspected, it will be confirmed by sterile speculum examination and testing of the amniotic fluid for ferning or nitrazine. The number and type of ECV maneuvers will be recorded. Bleeding, development of a vaginal hematoma, and delivery within an hour of performing the ECV procedure will be recorded.

Delivery Outcome (maternal):
Researchers will record the fetal presentation at labor admission, type of delivery, whether there was a shoulder dystocia, and the blood loss as measured by weighing any saturated sponges from the medical record.

Delivery Outcome (neonatal):
Researchers will measure the neonatal weight, 1- and 5-minute Apgar scores, whether the baby was stillborn, had a bone fracture, or was intubated and/or admitted to the neonatal intensive care unit from the medical record.

Length of Stay:
Researchers will record the length of stay for mothers for the ECV procedure, and length of stay for both mothers and neonates for the admission for delivery, all measured in hours.

Cost of Stay:
Researchers will record the cost of stay for both mothers and babies, for both the ECV procedure and the admission for delivery. This will be obtained from the mother's and child's medical record.

Data Management and Quality Plan

Data De-identification

Data will be de-identified prior to analysis. Each patient will be assigned a 4-digit code that will not contain any unique identifiers. The code will be linked to the patient's FIN which will be stored in a separate file on a password-protected laptop stored in a locked office. The de-identified data will be stored in a similar fashion in a separate file. Drs. Hill, Lense, the research department personnel and the honest broker will have access to both files. We anticipate that once data is entered for each individual patient, the link will be used only for the purposes of random audits to ensure data accuracy. Once data has been analyzed and results have been published, the link to the de-identified data will be destroyed after 7 years. As the assigned study number will not be linked to any PHI, we do not foresee any possible breach occurring.

Data Confidentiality, Storage, and Retention

Study documentation and paperwork will be stored behind 2 locked doors in the Center for Pediatric & Women's Research Department during the active study period. Upon study closure the paper records will remain in the research office for storage. The data file will be stored electronically on a password protected secure server at AdventHealth accessible only to study team members as listed on the personnel log. Study documentation will be retained for 7 years after study completion. After that period, paper records will be placed in hospital approved shred bins.

Electronic records will be placed in a computer electronic trash bin followed by immediate emptying of the electronic trash bin.

Data Quality

Quality control procedures for this study include source data verification by randomly selecting 10% of subjects (9 if enrollment goal is met) and verifying all values. If more than one discrepancy is found, an additional 10% of subjects will be checked. Based on those findings, additional subjects or all subjects may be verified. The AdventHealth Office of Research Integrity will create a monitoring plan and conduct internal monitoring of the study for patient safety and data integrity.

Clinical trial monitoring is conducted to ensure that the rights and well-being of trial participants are protected. Reported trial data are accurate, complete and verifiable.

Clinical trial monitoring will be conducted by AdventHealth Office of Research Integrity monitoring team to ensure compliance with all applicable federal and state regulations, ICH GCP E6 (R2) standards and approved protocol. This study will be monitored using a risk-based approached. A monitoring plan will be created to ensure patient safety, data quality and integrity is ongoing throughout the life of the study. The frequency and elements of monitoring will be outlined in the monitoring plan. The monitor will ensure study is conducted, recorded and reported as required by federal regulations and IRB of record. Monitoring will be conducted on-site and/or remote. After completion of site monitoring, a report will be provided to PI and study team. The PI and study team are required to review the report and work on significant findings or discrepancies to resolution. If any findings are required to be reported to the IRB, the PI will be made aware and prompted to self-report. All serious and continuing non-compliance is shared with the Research Oversight Committee who may require appropriate actions.

Protocol Deviations

All deviations and SAEs must be reported promptly to AH ORI and regulatory team. SAEs must be reported within 24 hours of discovery. Any SAE required to be reported to the FDA and IRB will be completed with the assistance of the central regulatory team in conjunction with the principal investigator and study team."

Data Sharing (outside of AdventHealth Orlando): N/A

Sample Size Determination

Based on prior studies of patients without regional anesthesia who had a success rate of approximately 49%, and assuming a 1:1 allocation of intervention and control subjects, with an 80% power, and a 2-sided 5% significance level, we calculated a sample of size of 69 in each group to increase the success rate from 49% to 73.5%. Assuming a 10% case dropout rate we will enroll 76 patients in each arm (152 total participants).

Statistical Analysis Plan

Primary Objective Analysis

The success of ECV procedures for the intervention group compared to the control group will be analyzed using chi-square and Fisher exact tests. A P value of <0.05 will be considered statistically significant.

Secondary Objective Analysis

Maternal and neonatal outcomes will be analyzed using chi-square and Fisher exact tests for categorical variables, unpaired t-tests for continuous variable, and non-parametric tests for continuous variables that are not normally distributed. P values <0.05 will be considered statistically significant.

Potential Risks and Benefits

Potential Benefits

The Fetal Pillow device may improve the ECV success rate.

Potential Risks

Although unlikely based on prior device usage during 2nd stage arrest, it is possible the device may cause vaginal bleeding, increased pain during the procedure, or either no change in success or a lower success rate compared to performing the procedure without the device. Terbutaline administration may cause maternal tachycardia, irritability, chest pressure or chest pain. While loss of confidentiality is a potential risk to patients, patient information will be de-identified prior to analysis and only study personnel will have access to patient information. The United States Food and Drug Administration has determined that this study protocol is a nonsignificant risk (NSR) study (Review # Q191927, notification received December 18, 2019).

Mitigation of Risks

Patients will be asked prior to administration of terbutaline if they have contraindications, which is standard practice prior to using this medication.

Provisions to Protect the Privacy Interest of Subjects

The steps to protect the privacy of subjects have been described previously. Briefly, study documentation and patient information will be stored in a separate file on a password-protected laptop stored in a locked office. Drs. Hill, Lense and research team will have access to both files.

Early Withdrawal of Subjects

Investigator Withdrawal of Subjects.

Inability to place Fetal Pillow: If the Fetal Pillow cannot be placed, for example due to pain, or the Fetal Pillow cannot be inflated, the patient will be withdrawn from the study. However, she may undergo an attempted ECV outside of the study protocol if she wishes.

Delivery at a hospital outside of the AdventHealth Orlando system: If the patient delivers outside of the AdventHealth Orlando system she will be withdrawn from the study analysis.

Subject Request for Withdrawal from Study

Patient requests withdrawal: Patients who request withdrawal for any reason will be immediately withdrawn. If a patient initially consents to have the Fetal Pillow placed, then changes her mind before or during the procedure, the researcher will remove the device and offer the patient the opportunity to proceed with an ECV attempt off-protocol. Researchers will ask the patient if they can complete data collection for delivery and proceed according to the patient's wishes. There are no known or suspected harms from withdrawing from the study.

Data Collection and Follow-up for Withdrawn Subjects

Patients electing to withdraw from the study will be asked if they consent to data collection for delivery. If they decline this, then data collection will discontinue, and the data collection sheet will be stored as deidentified data in case the patient's reason for withdrawal (for example, excessive pain) is identified as a side effect of the device. The percentage of patients withdrawing and the reasons for withdrawal will be calculated and included in any manuscript submissions.

Adverse Event Reporting

Adverse events will be collected from the time of insertion up to 1 hour after the ECV procedure and followed until discharge. Adverse events such as excessive pain or bleeding will be recorded as part of the data collection. Adverse events of special interest will be reported according to AdventHealth Orlando IRB policies

Adverse events of special interest include:

Term	Mild	Moderate	Severe	Serious	Serious

Vaginal Hemorrhage	Mild symptoms; intervention not indicated	Moderate symptoms; intervention indicated	Transfusion indicated; invasive intervention indicated; hospitalization	Life-threatening consequences; urgent intervention indicated	Death
Pelvic Hematoma	Mild symptoms; intervention not indicated	Minimally invasive evacuation or aspiration indicated	Transfusion; invasive intervention indicated	Life-threatening consequences; urgent intervention indicated	Death
Vaginal Laceration	Separation of the perineal skin only	Injury to the perineal muscles but not the sphincter or rectum	Injury to the perineal muscles and anal sphincter	Injury to the perineal muscles, sphincter, and rectal mucosa	Death
Premature ruptured Membrane	Confirmed rupture of membranes	Rupture of membranes leading to immediate discontinuation of ECV procedure	Rupture of membranes leading to immediate labor induction	Life-threatening consequences; Cord prolapse resulting in fetal harm, defined as umbilical artery PH < 5 or admission to NICU	Cord prolapse resulting in fetal death
Other	Mild symptoms; intervention not indicated	Minimal, local or noninvasive intervention indicated	Medically significant but not immediately life-threatening	Life-threatening consequences; urgent intervention indicated	Death

- Severity of an adverse event will be determined and classified as described above by the Investigator.

- An unanticipated adverse device effect: any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.3).
    - Sponsor will comply with FDA regulations 21 CFR 812.46 for monitoring requirements.

Relatedness/Causality of an adverse event will be determined and classified as described below by the Investigator.

Classification	Definition
Related	An event that results from the presence or performance (intended or otherwise) of the investigational device.
Unknown	An adverse event that cannot be determined to have a causal relationship with the device
Not Related	An adverse event that has been determined to not have a causal relationship with the device

Serious Adverse Event Reporting

A serious adverse event is defined as an adverse event "if, in the view of the investigator, it results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization*a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

*Planned hospitalization for a pre-existing condition, or a procedure required by the clinician that is not related to the device, will not be considered a Serious Adverse Event.

Only SAEs deemed related to the device will be reported electronically to the FDA and AHIRB no later than within 10 working days after the investigator first learns of the event (21 CFR 812.150(a)(1)).

Safety Monitoring Plan

Safety Monitoring

While we consider the project to be relatively low risk, there is always the possibility of adverse events. The safety monitoring plan will include: (1) review of interim analyses of outcome data; (2) review of reports of related studies to determine whether the monitored study needs to be changed or terminated; (3) review of major proposed modifications to the study prior to their implementation; and (4) provide the study leadership with written recommendations concerning the trial including continuing, changing or terminating the study. Safety monitoring will occur after the first 10 randomized subjects and every 20 subjects thereafter. Rachel Humphrey M.D., Chair of Fetal Medicine Department and Vicki Smith R.N., Nurse Manager Labor and Delivery Unit will conduct the safety monitoring plan.

Data and Safety Monitoring Board (DSMB) or Equivalent: N/A

Ethical Considerations

N/A

Sharing of Results with Subjects

Patients will be immediately aware if the ECV procedure was successful. Upon completion of study data analyses, subjects will have the option to contact study team to obtain their randomization arm information.

Funding Source

There is no external funding for this research. The manufacturer of the Fetal Pillow has agreed to supply devices and have not been involved in the study design.

Subject Stipends or Payments: *N/A*

Publication Plan

The plan is for presentation and publication of the study findings. The roles and responsibilities of each research team member have been determined, and assignment of authorship has occurred. ICMJE guidelines have been followed.

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