Title: Evaluation of Hysterotomy Site After Open Fetal Surgery

IRB#: FCI-22581

NCT02493062

Responsible Party: Dr. Laura Vricella

Date of Document: 12/20/17

Protocol Title: Evaluation of Hysterotomy Site after Open Fetal Surgery
Protocol Status: CLOSED
Date Submitted: 06/15/2017
Approval Period: Draft
Important Note: This Print View may not reflect all comments and contingencies for approval. Please check the comments section of the online protocol. Questions that appear to not have been answered may not have been required for this submission. Please see the system application for more details.

* * * Amendment * * *

Amendment

Complete this form and with it, submit any affected IRB materials needing revision. Please provide the entire revised documents (not just revised pages). Protocol amendments must receive IRB review and approval before they are implemented, unless an immediate change is necessary to eliminate an apparent hazard to the subjects.

1. **Number of accrued subjects** 35

2. **Status of Study (check one):**
   - Continuing to accrue study subjects.
   - X Closed to accrual. Date closed: 05/22/2017

3. **Special populations (mark as applicable):**
   - Children (<18 years of age)
   - Prisoner population targeted or study participant became a prisoner

4. **Summarize the proposed changes to the protocol in lay terms, including the type of change AND what the change involves.**

   If this is a change in PI a new Department Chair review is required. Please upload the signed document in the Attachments section.

   Adding personnel.
   Removing personnel.
   Changing PI.

5. **Provide justification/explanation for the proposed changes.**

   Chase Pribble, SLU Medical Student, added to protocol.
   Dr. Mike Vlastos removed from personnel. No longer with Saint Louis University as of June 30, 20117.
   Dr. Laura Vricella added as PI.

6. **For sponsor amendments, when did the SLU site receive notification of changes?** X N/A

7. ** Will currently accrued subjects need to be notified of changes?** Y

   If no, please justify why not.

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If yes, please explain how AND when notification or re-consenting will occur.

participants who are still in follow-up will be sent a letter informing them of the change in PI

8. Does the SLU IRB Protocol need to be modified? **N**

9. Are consent documents modified? **N**

Proceed to the appropriate section(s) of the protocol and make your changes. Also make necessary changes in the Consent Form(s), Assent Form(s), Recruitment Statement, or other attachments, as applicable. Use track changes or highlight (in yellow) changes to documents being revised. Please upload a tracked/highlighted copy of each revised document to be stamped upon IRB approval.

NOTE: Upload a clean copy (changes or highlights removed) of documents in file formats other than Microsoft Word (i.e., the IRB will remove the tracked changes/highlights on uploaded Word documents).

NOTE: Protocol amendments must receive IRB review and approval before they are implemented, unless an immediate change is necessary to eliminate an apparent hazard to the subjects.

Sponsored Studies: Remember to update the Sponsor's Protocol version number and date in the Funding section of the protocol (this information will appear on the approval letter).

List of changed sections:
Attachments (16)

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* * * Subject Population * * *

Subject Population(s) Checklist

Select All That Apply :

- [X] Adults
- [ ] Cognitively Impaired Subjects
- [ ] Employees (specifically targeted)
- [X] Fetuses
- [X] Minors (under 18)
- [X] Neonates
- [ ] Non-English Speaking Subjects
- [ ] Pregnant Women
- [ ] Prisoners
- [ ] Students (specifically targeted)
- [ ] Terminally Ill Subjects
- [ ] Wards of the State
- [ ] Other (any population that is not specified above)

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* * * Study Location * * *

Study Location(s) Checklist

Indicate where the study will be conducted. Select all that apply:

- [ ] Saint Louis University, Medical Center Campus
- [ ] Saint Louis University, Frost Campus
- [ ] Saint Louis University, Madrid Campus
- [ ] Saint Louis University, UMG Practice Locations
- [X] SSM STL (DePaul Hospital, St. Mary's Health Center, St. Joseph (St. Charles, Wentzville, Lake Saint Louis), St. Clare)
- [X] Cardinal Glennon Children's Medical Center
- [ ] Saint Louis University Hospital (SSM Health- SLU Hospital)
- [ ] SLU-SSM Cancer Center Research Alliance Sites
- [X] Other (In the box below, list any off-campus institutions or locations and describe the activities being conducted there. Please provide letters of cooperation and/or IRB approvals from each location to document support/approval of the study. You may provide such documentation as it becomes available, but you may not begin work at those sites until documentation of support is provided to the IRB.) Please refer to the Guidance for involving non-SLU institutions in human subject research.

The Sonohystergrams being performed at SSM STL at St. Mary's Health Center in the Bellevue Office (SLUCare Maternal Fetal Medicine office, 4th floor).

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* * * General Checklist * * *

General Checklist

Select All That Apply :

- [ ] Collection of Specimens
- [ ] Data collection via e-mail or the Internet
- [ ] Deception/Incomplete Disclosure
- [ ] Dietary Supplements, Vitamins, and Other Food Agents
- [X] FDA Approved Device
- [X] FDA approved drugs, reagents, other chemicals administered to subjects (even if they are not being studied), or biologic products
- [ ] Genetic Testing
- [ ] HIV Testing
- [ ] Human blood, cells, tissues, or body fluids
- [ ] International Research or Research on International Populations
- [ ] Investigational drugs, reagents, chemicals, or biologic products
- [ ] Investigational Device
- [X] Investigator Initiated Study *?HELP?*
- [X] Medical Records
- [X] Photography, Video, or Voice-Recording Subjects

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X Questionnaires and/or tests
Radioisotopes/radiation-producing machines, even if standard of care
rDNA/Gene Transfer Therapy
Registry(ies)
Specimens to be stored for future research projects (must be in consent form)
Study of existing data or specimens
X University Indemnified Study (SLU is responsible for liability coverage) *?HELP?*
Other (clarify in text box to the right)

Single Use. Provide a brief summary and justification for the Single Use Therapy. Note: This application will refer to research. For Single Use applications it is understood that 'research' will mean 'therapy'.

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* * * Funding * * *

Funding Checklist

NONE

Funding - Other

Name of Other Funding source	SLU eRS #
SSM St Mary's Foundation	61223

NOTE: Applicable grant application, contract or subcontract, investigator's brochure, and sponsor's protocol (for all industry sponsored clinical trials) must be attached. You will be prompted for these in section #16 (Attachments).

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* * * Expedited Paragraphs * * *

To request an Expedited Review, check the appropriate category(ies) below. Provide justification for your request for Expedited Review.

To qualify for expedited review, research activities must (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the categories below.

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

a) **Research on drugs for which an investigational new drug application (21 CFR Part 31, 32) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)**

b) **Research on medical devices for which**

(i) An investigational device exemption application (21 CFR Part 812) is not required; or

(ii) **The medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.**

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

a) **From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or**

From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

Children are "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted."

3. Prospective collection of biological specimens for research purposes by non-invasive means.

EXAMPLES: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra-and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving X-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited

review, including studies of cleared medical devices for new indications.)

EXAMPLES: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subjects' privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiology; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

8. [FOR IRB use only]. Continuing review of research previously approved by a convened IRB only when condition (a), (b), or (c) is met.

   a) Previously approved research where
      (i) The research is permanently closed to the enrollment of new subjects;
      (ii) All subjects have completed all research-related interventions; and
      (iii) The research remains active only for the long term follow-up of subjects.

   b) Previously approved research where no subjects have been enrolled and no additional risks have been identified.

   c) Previously approved research where the remaining research activities are limited to data analysis.

9. [FOR IRB use only]. Continuing review or research not conducted under an investigational new drug application or investigational drug exemption where expedited categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

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* * * Background, Purpose, Study Procedures * * *

Title

Evaluation of Hysterotomy Site after Open Fetal Surgery

Complete Sections 1 - 16. In sections that allow reference to sponsor protocol or grant, clearly state section and page numbers. Any information that is different or specific to the local site should be in the SLU application. Specify N/A as appropriate. Do not leave any required sections blank.

1. Background

Page numbers from a sponsor's protocol/grant may be referenced in 1a and 1b.

a) **Provide an introduction and background information. Describe past experimental and/or clinical findings leading to the formulation of the study, if applicable. Investigator Initiated studies must cite references in the response provided or attach a bibliography. *<a href="javascript:showPopUpdata('HELP','Application Consideration:**

In this question the IRB requires a brief introduction with supporting background information to describe your study. Do not include overly lengthy descriptions.

Investigator Initiated studies (i.e., the Principal Investigator has conceived, designed, and is conducting the research) are required to cite references in the response or should upload a referenced bibliography in the Attachments section.')">?HELP?*

Open fetal surgery improves outcomes for infants.1 Open fetal surgery is used to complete the repair of Myelomeningocele, EXIT procedures, repair of some lung masses, and some sacral coccygeal teratomas. Maternal Fetal Surgeons accomplish fetal surgeries by performing a hysterotomy, using a staple gun, 2 to attach all the layers together and decrease maternal bleeding . Opening the uterus in this manner requires the mother to have a cesarean section for this pregnancy and all future pregnancies.
Vikhareva used an ultrasound method (sonohysterogram)that puts a small amount of liquid in the uterus, producing images to better define the thickness of the uterine scar.3 His team documented on women who had Cesarean Sections at birth.
In open fetal surgeries the infant's problem (MMC, CCAM, SCT) is repaired. The fetus is placed back into the uterus to grow. The infant stretches, kicks the uterine wall and the hysterotomy site until time for delivery. Dr. Vlastos wants to use the same ultrasound method and look at the uterus 6 or more months after delivery of all women evaluated by St. Louis Fetal Care Institute at Cardinal Glennon and who have received open fetal surgery. The sonohysterogram can measure the size and depth of the uterine scar allowing better predictive values for future pregnancies.4

1.Gupta, N, etal. Open fetal surgery for myelomeningocele, A review. Journal Neurosurgical Pediatrics 9: 265-273, 2012
2.http://www.drpankajdesai.com/IA/2.htm
3.Vikhareva, Osser, etal. Clinical importance of appearance of cesarean hysterotomy scar at transvaginal ultrasonography in nonpregnant women. Obstetrics and Gynecology. 2011 Jun;117(6):1438.
4.http://www.radiologyinfo.org/en/info.cfm?pg=hysterosono#part_one

Please save frequently

b) **Describe any animal experimentation and findings leading to the formulation of the study, if**

there is no supporting human data.

none

2. Purpose of the study

a) **Provide a brief lay summary of the project in <200 words. The lay summary should be readily understandable to the general public.**

This study is to review how your uterus has healed after having open fetal surgery of your child and yourself. Your uterus now has a scar (perhaps two: one from the open fetal surgery and a second from delivery by cesarean section; rarely, the same area of your uterus was used for both open fetal surgery and delivery). From other studies of surgery performed on a uterus, some of the uterine scars do not heal well. This study uses sterile saline (water-like liquid which is sterile) to spread open the inside of the uterus. The saline is placed with a small catheter placed into the uterus with you positioned similar to that of having a Pap smear. The saline is slowly placed into the uterus as an ultrasound is performed to take pictures of the uterus, its inside and the walls. In this way, the healed areas from the uterine surgery can be seen with ultrasound and evaluated. This is performed at least 6 months after your delivery and, of course, knowing you are not pregnant at the time of the test. A urine pregnancy test will be performed prior to the study.

Page numbers from a sponsor's protocol/grant may be referenced in 2b and 2c.

b) **List your research objectives (specific aims & hypotheses of the study).**

Primary Outcome:
Measure the depth of the scar and location of the scar 6 months or longer after delivery

Secondary Outcomes:
Measure length of hysterotomy at the time of open surgery
Number of days post op until delivery
Open fetal surgery hysterotomy at the time of delivery
Monitor of future pregnancy(ies)
- fertility (planned or unplanned), length of gestation, prior hysterotomy condition (uterine incision created at the time of open fetal surgery) at the time of future delivery, complications from potential uterine dehiscence/rupture.
- fertility concern for having undergone an invasive uterine procedure: evaluation of patient concerns for future pregnancy(ies) and depression.

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c) **Describe the study design (e.g., single/double blind, parallel, crossover, control, experimental, observational, etc.). If the study is investigator-initiated, a timeline for individual subject recruitment, follow-up, and analysis for the study is required. Also, indicate if the subjects will be randomized.**

This is an Investigator initiated, prospective study reviewing medical records and performing a sonohysterogram on non-pregnant women at 6 or more months after delivery of an infant who received open fetal repair.

d) **If subjects will be given placebo, please justify placebo use. *?HELP?***

n/a

3. Study Procedures

a) **N** Is this project a multicenter study (i.e., same project is conducted elsewhere by a different investigator) OR does this study involve conduct of research at multiple sites?

Is SLU acting as a coordinating center for other sites OR is the SLU PI a direct recipient of a federal grant for this research? If yes, complete and attach the Supplemental Application for Coordinating Center Activities.

Will the SLU site be participating in all parts/procedures/arms of the study?

If No, explain what SLU will NOT participate in:

Please save frequently

Page numbers from a sponsor's protocol/grant may be referenced in 3b, 3c, and 3d.

b) **Describe all the procedures, from screening through end-of-study, that the human subject must undergo in the research project, including study visits, drug treatments, randomization and the procedures that are part of standard of care. Specify which procedures are for research and which are standard of care. Please note: The box below is for text only. If you would like to add tables, charts, etc., attach those files in the Attachment section (#16).**

•An evaluation is completed at SSM Cardinal Glennon (CG), Fetal Care Institute (FCI) of a woman who has decided to have open fetal surgery to complete a fetal repair before the infant is born. (SOC)
•She will be approached in the FCI clinic setting by a member of the research team.
•This study will be discussed and all questions answered. If concerns persist they will be referred to Dr. Vlastos for clarification.
•The Study consent and HIPAA authorization will be signed.
•After open surgery she will be monitored and delivered appropriately, maintaining SOC.
•After the infant is born we will review the mother's and infant's electronic health records and FCI database records. (The datasheet is attached with the data points.) Gathering SOC information.
•She will be contacted by phone five months after giving birth and have a telephone interview by a member of the research team. This is part of the research plan and the list of conversational questions is attached. An appointment will be made for her to return for a sonohysterogram. (SLU Care IRB department is the SLU IRB or SSM Cardinal Glennon Fetal Care Institute)

•A reminder letter may be sent 2 weeks before appointment and a reminder phone call may be completed the day before the appointment.
•6 months or more after delivery of an infant who has received open fetal repair the women will have a sonohysterogram to evaluate the healing process.
i.600 mg of ibuprofen should be taked 1 to 2 hours before the procedure.
ii preferred timing is 1 week after menses.
iii.A transcervical catheter is inserted in the uterus.
iv.Small amount (approximately 20 ml to 100 ml) of sterile saline in introduced into the uterus.
v.Ultrasound is used to evaluate the hysterotomy site.
•After the sonohysterogram the data sheet will be completed and information will be shared with the women. (Experimental)
Annual phone calls are made to the women to monitor pregnancy status until the conclusion of

the study. (Experimental
If a pregnancy has occurred get a copy of the health and physical report(H&P) and the delivery report. (Experimental)

c) **If the proposed study is a clinical trial where a drug, vaccine, device or other treatment is compared to a placebo group or comparison treatment group, what are the guidelines or endpoints by which early decisions regarding efficacy or lack of efficacy can be made? For example, it may be reasonable to stop enrollment on a study when efficacy has already been clearly demonstrated, to avoid unnecessary enrollments of additional subjects. Alternatively, it may be reasonable to stop enrollment when it is clear that efficacy will never be demonstrated, given the statistical power of the study as designed. Describe the guidelines that are in place to assist in making these determinations, if relevant to the proposed study.**

n/a

d) **Describe how data analysis will be performed (statistical tests, methods of evaluating data) and indicate the smallest group/unit for which separate reporting will occur. For studies involving a questionnaire, if data and reliability information are available, please describe or provide references. For full board, unfunded studies describe sample size determination and power analysis. If none, please justify.**

Data will be collected from patient interview/questionnaire (by phone). Data collection will be transcribed to an Excel spreadsheet. Data will be now be transcribed to REDCap.
Each patient will have separate reporting.
All patients will be used for this descriptive study.
Continuous data (thickness of uterine wall: myometrium) will analyzed for average, mean, maximum and minimum and correlated with any known complications: dehiscence/rupture/repair at cesarean delivery.
Numerical data similarly.
Collected data will be analyzed using standard statistical methods. (averages, mean, max, min).

Please save frequently

e) **State if deception (including incomplete disclosure of study purpose/procedures) will be used. If so, describe the nature of the deception and provide a rationale for its use. Also, describe debriefing procedures or justify a waiver of the requirement to debrief. NOTE: for studies using deception, an alteration of consent must be justified in the Informed Consent section of the protocol (#13) and the debriefing script/statement must be uploaded in the Attachments section (#16). <a href=http://www.slu.edu/Documents/research/irb/Deception_Incomplete.doc target=_blank > See IRB Deception Guidelines.**

f) **Is there an accepted standard of care and/or standard practice at SLU for the condition/disease/situation being studied? This information will assist in comparing the risk/benefit ratio of study procedures relevant to usual care that would be received outside of the research context. *?HELP?*** Y

If yes, please describe the standard of care and standard practice at SLU for the condition/disease/situation being studied.

After open fetal surgery all future pregnancies must be by cesarean section.

Stand of care (SOC) after open fetal surgery is, at this time, no different than that of a cesarean delivery: physician visits at 1 - 2 weeks postpartum and at 6 weeks (the close of the puerperium). At this time, sonohysterogram is not within the SOC. However, having attending international meetings regarding open fetal interventions, the maternal risks at the index procedure and future pregnancies is always highlighted. At the recent Society of Maternal Fetal Medicine meeting (February 2013), one center provided statistics on the open fetal hysterotomy status at the time of delivery: 28% complication rate was shown: dehiscence and/or rupture. This is unpublished data.

g) **Does this study involve any diagnostic imaging, labwork or genetic testing that could result in clinical discovery (diagnoses, genetic mutations, etc.)? Note that this could include discovery that is expected (related to the research) or incidental (not related to research aims, but possible, like a mass/shadow found in imaging despite not looking for it).** N

If yes, please describe and include whether there are plans to share findings with study participants.

h) **Is this study subject to the NIH Genomic Data Sharing Policy?** N

The NIH GDS policy applies to all NIH-funded research that generates large-scale human genomic data as well as the use of these data for subsequent research and includes: genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, metagenomics, epigenomic and gene expression data, irrespective of NIH funding mechanism. Click here for more specific examples.

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* * * Radioisotopes or Radiation Machines * * *

You have not selected the Radioisotopes option in the General Checklist. If you would like to add Radioisotopes information, please select the option to enable this section.

4. Radioisotopes or Radiation Machines

In this section, investigators must enter all radiation usage associated with the protocol.

Important: Protocols that involve non-standard of care radioactive materials (which includes the terms "radioisotopes", "radionuclides", "radiopharmaceuticals", and "nuclear medicine studies", e.g., "PET", "MUGA", "Zevalin", and/or specific radionuclides such as "F-18", "Tc-99m", "Th-201", "I-131", "Ra-233", "Y-90", etc.) will receive review by the Radiation Safety Officer (RSO) and/or Radiation Safety Committee (RSC). In these cases, submission to the RSO/RSC should occur first, even before submission to IRB. For more information on how to submit for radiation safety review, see RSC instructions or contact the Radiation Safety Officer at 977-6895.

(1) It is the responsibility of the PI to assure the accuracy and completeness of the data submitted in this section, consistent with guidelines provided below. (2) For projects requiring radiation procedures, please refer to this guidance.

a) **If applicable, list and quantify the radiographic diagnostic and therapeutic procedures associated with**

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this protocol by clicking "Add" and adding to Table 1 below. (Includes X-ray, fluoroscopy, CT, radioactive materials, nuclear medicine, PET-CT, radiation oncology, accelerator, Cyber Knife procedures, etc.)

b) Total estimated research radiation dose * :

* Calculate from the table above by adding the Effective Dose Subtotals for all procedures.

NOTE: Informed Consent Radiation Exposure Risk Statement- The applicant must insert the appropriate Informed Consent Radiation Exposure Risk Statement template language into the SLU IRB Informed Consent, inclusive of applying the total estimated research radiation dose specified in item b) from the table above, as instructed in the SLU IRB Informed Consent Template. Contact the IRB Office at 977-7744 or irb@slu.edu with any questions.

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* * * Devices * * *

5. Devices

a) Please list in the space below all investigational devices to be used on subjects during this study.

b) Please list in the space below all FDA approved devices to be used on subjects during this study.

FDA Approved Devices

Device Name	Manufacturer	Provide IDE #. Documentation of IDE # required unless imprinted on sponsor protocol (attach in section #16).
Sonohysterogram		

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* * * Drugs, Reagents, Chemicals, or Biologic Products * * *

6. Drugs, Reagents, Chemicals, Biologic Products, or Dietary Supplements, Vitamins, and Other Food Agents

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Pilot	Phase I	Phase II
Phase III	Phase IV	X Not Phased

List placebo if it is considered a drug (contains more than inactive ingredients). For example, normal saline is considered a drug that should be listed, whereas placebo tablets are usually inert ingredients that do not need to be listed.

** b) Please list in the space below all investigational drugs, reagents or chemicals to be administered to subjects during this study. Attach all applicable Investigator Brochures in section #16 (Attachments).**

** c) Please list in the space below all FDA approved drugs, reagents, chemicals to be administered to subjects during this study. Attach all applicable package inserts in section #16 (Attachments).**

FDA Approved Drugs, Reagents, Chemicals, Biologic Product

Drug Name	Manufacturer	Source (e.g., Pharmacy, Sponsor, etc.)	Dosage
Sterile saline solution	Numerous	Pharmacy	20 - 100 ml
ibuprofen	assorted	pharmacy of mother's choice	600 mg

** d) Please list in the space below all dietary supplements, vitamins, minerals, or foods to be administered to subjects during this study.**

Please read the IND Statements.

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* * * Other Levels Of Review * * *

7. Other Levels Of Review

1. University Radiation Safety

Protocols that involve non-standard of care radioactive materials (which includes the terms "radioisotopes", "radionuclides", "radiopharmaceuticals", and "nuclear medicine studies", e.g., "PET", "MUGA", "Zevalin", and/or specific radionuclides such as "F-18", "Tc-99m", "Th-201", "I-131", "Ra-223", "Y-90", etc.) will receive review by the Radiation Safety Officer (RSO) and/or Radiation Safety Committee (RSC). For information on how to submit for radiation safety review, see RSC instructions or contact the Radiation Safety Officer at 977-6895.

X **Not Applicable**

Yes, study involves radioactive materials (per instructions, submit to RSC before IRB)

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2. Institutional Biosafety

Experiments involving the deliberate transfer of Recombinant or Synthetic Nucleic Acid Molecules (e.g., Gene Transfer), or DNA or RNA derived from Recombinant or Synthetic Nucleic Acid Molecules, or Microorganisms containing Recombinant or Synthetic Nucleic Acid Molecules and/or infectious agents (including select agents and toxins as defined by CDC and/or Animal and Plant Health Inspection Service (APHIS)) into one or more human research participants must be reviewed by the SLU Biological Safety Officer. Most of these protocols also require review and approval by the SLU Institutional Biosafety Committee (IBC). Please contact the SLU Biological Safety Officer at 977-6888 for more information.

X **Not Applicable**

Yes, study requires Institutional Biosafety review

3. Pharmacy, Therapeutics, Nutrition, and Transfusion (PTNT) Committee

Saint Louis University Hospital requires that all research involving the administration of medications within the hospital (including outpatient areas such as the Emergency Department, Outpatient Center, Saint Louis University Hospital-South Campus, etc.) be reviewed and approved by the Pharmacy, Therapeutics, Nutrition, and Transfusion (PTNT) Committee and that study drugs are received, stored, prepared, and dispensed by the Hospital's Department of Pharmacy Services. Please contact the Investigational Drug Services Clinical Pharmacist at 268-7156 or SLUH-IDS@ssmsluh.com for more information.

X **Not Applicable**

Yes, study requires PTNT review

4. Saint Louis University Hospital

All research involving Saint Louis University Hospital, including inpatient or outpatient services and medical record access, requires approval from the Saint Louis University Hospital Research Review Committee prior to study initiation. This effort is coordinated through the Clinical Trials Office via eRS. This process is designed to facilitate compliance with state and federal regulations as they pertain to research in hospitals and clinical research billing. Documents should be submitted as soon as possible, or at the latest, concurrently with IRB submission. Please contact the Research Compliance Office at 577-8113 or sluh.research@ssmsluh.com or the SLU Clinical Trials Office at 977-6335 or clinical-trials-office@slu.edu for more information.

X **Not Applicable**

Yes, study requires Saint Louis University Hospital review

5. SSMSL

All research involving SSMSL locations (including Cardinal Glennon), including inpatient or outpatient services and medical record access, requires approval from the SSM STL or SSM Cardinal Glennon Research Business Review (RBR) prior to study initiation. This process is designed to facilitate

compliance with state and federal regulations as they pertain to research in hospitals and clinical research billing. While researchers can begin to complete the SSM RBR form at any time, the form should not be submitted until the IRB and the CTO have approved the study. Please contact the SSMSL Office at 989-2058 or Marcy.Young@ssmhealth.com for more information.

Not Applicable

X Yes, study requires RBR review

6.   Does this project require registration on ClinicalTrials.gov, and/or is this project subject to the NIH GCP Training Requirement? (Select "Yes" if either apply) Y

Registration may be required if any of the following apply: 1) The project meets the FDAAA definition of an "<a href=https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf target=_blank>Applicable Clinical Trial", which requires registration on ClinicalTrials.gov.; 2) As of January 1, 2017, a new NIH policy mandated biomedical and behavioral "Clinical Trials" to be registered on ClinicalTrials.gov. In addition, NIH policies require personnel on NIH "Clinical Trials" to take GCP Training every three years.; 3) Registering may be required for Journal Publication (ICMJE). Please review relevant definitions <a href=http://slu.edu/Documents/research/IRB/NIH_Clinical_Trial_Definition.docx target=_blank>here. Contact the CTO at clinical-trials-office@slu.edu with questions about registering on ClinicalTrials.gov and refer to the <a href=https://www.slu.edu/division-of-research-administration-home/institutional-review-board-(irb)/training-and-education target=_blank>Training page of the IRB website for information on NIH GCP Training requirements.

* * * Subject Population * * *

8. Subject Population - In the space below, please detail the participants that you are requesting to recruit (include description of each group requested)

a) Expected age range of subjects. (For example ≥ 18 yrs to 90 yrs).

>= 18 yrs. and <=50 yrs. and their infants
If a woman < 18 years old presented with a fetal tumor requiring open fetal repair, this would be done if deemed ethically sound by both CGCMC and SMHC ethics committees. Given this, then the patient may qualify for this study. This is a RARE event.

b) Number of evaluable subjects to be accrued at SLU or SLU site (this includes all sites under the direction of the SLU PI). 100 mothers and 100 infants

Exceeding the number listed here is a protocol violation. Prior IRB approval is required if additional participants are to be accrued. If applicable, this number should be consistent with your power analysis described in 3d.

c) Number of evaluable subjects to be accrued study wide. *?HELP?* 100 mothers and 100 infants

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d) **If including vulnerable populations (<a href=https://www.slu.edu/Documents/research/IRB/Minors_in_Research.doc target=_blank>minors, <a href=https://www.slu.edu/Documents/research/IRB/Pregnant_Women_Fetuses.docx target=_blank>pregnant women and fetuses, <a href=https://www.slu.edu/Documents/research/IRB/Neonates.docx target=_blank>neonates, <a href=https://www.slu.edu/Documents/research/IRB/Non-English_Speaking_Subjects.doc target=_blank>non-English speaking, economically or educationally disadvantaged, <a href=https://www.slu.edu/Documents/research/IRB/Prisoner_Research.doc target=_blank>prisoners, <a href=https://www.slu.edu/Documents/research/IRB/Adults_Unable_to_Provide_Consent.docx target=_blank>adults temporarily or permanently unable to consent for themselves): 1) provide the rationale for the importance of including this population in the research, and 2) specify the measures being taken to minimize risks to potentially vulnerable subjects. Click on hyperlinks to access <a href=https://www.slu.edu/division-of-research-administration-home/institutional-review-board-(irb)/general-guidelines target=_blank>SLU Guidelines containing additional considerations and strategies for mitigating risks.**

Since the study is a result of a fetal intervention, it is inherent to include fetuses and pregnant women.

If a woman < 18 years old presented with a fetal tumor requiring open fetal repair, this would be done if deemed ethically sound by both CGCMC and SMHC ethics committees. Given this, then the patient may qualify for this study. This is a RARE event.

e) **If women, minorities, or minors are not included, a clear compelling rationale must be provided unless not applicable. Examples for not including minors: disease does not occur in children; drug or device would interfere with normal growth and development; etc. If federally funded reference appropriate section of the sponsors protocol/grant. *?HELP?***

This is secondary to the myelomeningocele protocol; women must be 18 years old or older. However, if a woman < 18 years old presented with a fetal tumor requiring open fetal repair, this would be done if deemed ethically sound by both CGCMC and SMHC ethics committees. Given this, then the patient may qualify for this study. This is a RARE event.

f) **If any specifically targeted subjects are students, employees, or laboratory personnel, specify the measures being taken to minimize the risks and the chance of harm to these potentially vulnerable subjects. See <a href=https://www.slu.edu/Documents/research/IRB/Students_Employees.docx target=_blank>SLU Guidelines for additional considerations and strategies for mitigating risks.**

g) **Describe how potential subjects will be identified for recruitment (e.g., chart review, referral from individual's treating physician, those individuals answering an ad). How will potential participants learn about the research, and how will they be recruited (e.g., flyer, e-mail, web posting, telephone, etc.)? Upload recruitment materials in the Attachment Section (#16). Important to remember: potential subjects cannot be contacted before IRB approval. NOTE: The use of SLU owned websites in an approved SLU format (e.g., Cancer Center website, etc.) are always approved methods of recruitment.**

Subjects are referred to CG FCI by their OB or MFM for evaluation and consultation regarding their infant's abnormality. Women will be recruited for this study if they receive open fetal repair of that abnormality. A member of the research team will explain the study and answer all their questions. Women will be referred to Dr. Vlastos if questions or concerns persist.

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* * * Subject Population * * *

8. Subject Population (continued)

Page numbers from a sponsor's protocol/grant may be referenced in 8h.

h) Inclusion and Exclusion Criteria.

Identify inclusion criteria.

FCI evaluation
Received Open Fetal Surgery
Open fetal surgery of myelomeningocele: maternal age of >= 18 yrs. and <=50 yrs.
If a woman < 18 years old presented with a fetal tumor requiring open fetal repair, this would be done if deemed ethically sound by both CGCMC and SMHC ethics committees. Given this, then the patient may qualify for this study. This is a RARE event.
Agree to travel to Saint Louis for sonohysterogram 6 or more months after delivery.

Identify exclusion criteria.

Presently pregnant
Hysterectomy after delivery
Menopause
Using IUD (Intrauterine Device) for birth control
There is no exclusion criteria for infants

i) Compensation. Explain the amount and schedule of compensation, if any, that will be paid for participation in the study. Include provisions for prorating payment.

You will not be paid to take part in this study. However, travel and lodging expenses will be covered up to 400 dollars.
Travel distances will be calculated using Google maps.

If your primary residence is 50 miles or less you will receive a $50 dollar VISA card.
If your primary residence is 51 to 100 miles you will receive a $100 dollar VISA card.
If your primary residence is 101 to150 miles you will receive a $150 dollar VISA card.
If your primary residence is 151 to 200 miles you will receive a $200 dollar VISA card.
If your primary residence is 201 to 250 miles you will receive a $250 dollar VISA card.
If your primary residence is 251 to 300 miles you will receive a $300 dollar VISA card.
If your primary residence is 301 to 350 miles you will receive a $350 dollar VISA card.
If your primary residence is 351 miles or greater you will receive a $400 dollar VISA card.

The costs of sonohysterogram and the pregnancy test used in this research study are provided at no cost to you or your insurance carrier. The costs are covered by a grant from the SSM Health St. Mary's Foundation and the Saigh Foundation.

Annual phone calls are made to you by a member of the research team to monitor pregnancy status until you become pregnant, have a hysterectomy or approach menopause.

j) Describe who will cover study related costs. Explain any costs that will be charged to the subject.

The costs are covered by a grant from the SSM Health St. Mary's Foundation and the Saigh Foundation, no costs will be charged to the subject. All study procedures and tests will be covered by SSM Health St. Mary's Foundation and the Saigh Foundation Grant including sonohystograms and pregnancy tests.

k) Estimate the probable duration of the entire study including data analysis and publication. This estimate should include the total time each subject is to be involved and the duration the data about the subject is to

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be collected. If the study is Investigator-initiated, a timeline for individual subject recruitment, follow-up, total time for subject accrual, and data analysis for the study is required.

Subjects will be accrued for this study for 5 years maybe longer. We would like to follow subjects until they have another pregnancy, sterilization (a hysterectomy) or begun menopause. Completion of the study will take another 6 months. Analysis will take an additional year. Writing and publishing will take another year. We anticipate completion January 1, 2020.

It is intended that this study continue to move forward with patients throughout the existence of open fetal surgery at FCI. Similarly, if funding ends, the study would stop. Subjects will be accrued for this study in an ongoing manner. We anticipate annually accruing 15 new mothers participating in this study. We arbitrarily set the end date at 2020, however we may make an addendum to continue this study at that time.

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* * * Risks * * *

9. Risks

There is no research that can be considered totally risk free (e.g., a potential risk of breach of confidentiality). Therefore, when describing the risk, the lowest level of risk is "no more than minimal risk".

Page numbers from a sponsor's protocol/grant may be referenced in 9.1, 9.2, 9.3, and 9.4.

1.   Use of investigational devices. Please include the clinical adverse events (AEs) associated with each of the devices with an indication of frequency, severity and reversibility. This information can often be found in the Investigator(s) brochure. NOTE: Include any likely adverse effects associated with procedures that subjects may experience while in the study.

2.   Use of investigational drugs. Please include the clinical AEs associated with each of the drugs with an indication of frequency, severity and reversibility. This information can often be found in the Investigator(s) brochure. NOTE: Include any likely adverse effects associated with placebos or washout periods that subjects may experience while in the study.

3.   Use of FDA approved drugs, reagents, chemicals, or biologic products. Please include the clinical AEs associated with each of the drugs with an indication of frequency, severity and reversibility. This information can often be found in the package insert provided by the manufacturer. NOTE: Include any likely adverse effects associated with placebos or washout periods that subjects may experience while in the study.

There is a small, estimated at < 1%, risk of infection from sonohysterogram performance. The procedure is done with sterile saline, a sterile sonohystergram catheter and after cleansing the cervix with sterile saline. It is known both the intracervical canal and intrauterine space have endogenous

with sterile saline. It is known both the intracervical canal and intrauterine space have endogenous organisms. Hence, the sterile technique is utilized to minimize exposure of non-endogenous flora.

One dose of ibuprofen would be expected to have minimal risks; common side effects include abdominal pain, acid or sour stomach, heartburn, indigestion, itching skin, nausea, dizziness, ringing in the ear, and rash. It is suggested to take any ibuprofen with a small amount of food. Fundamental risk of hypersensitivity reaction for those who have not taken ibuprofen before may occur.

4.   Use of FDA approved devices. Please include the clinical adverse events (AEs) associated with each of the devices with an indication of frequency, severity and reversibility. This information can often be found in the Investigator(s) brochure. NOTE: Include any likely adverse effects associated with procedures that subjects may experience while in the study.

There is a small, estimated at < 1%, risk of infection from sonohysterogram performance. The procedure is done with sterile saline, a sterile sonohystergram catheter and after cleansing the cervix with sterile saline. It is known both the intracervical canal and intrauterine space have endogenous organisms. Hence, the sterile technique is utilized to minimize exposure of non-endogenous flora.

5.   Describe any risks related to performing study procedures. Please include all investigational, non-investigational, and non-invasive procedures (e.g., surgery, blood draws, treadmill tests).

Ultrasound is a painless procedure which uses only sound waves to examine the uterus. Local anesthesia is generally not necessary for a sonohysterogram. The patient may experience some mild cramping as the catheter balloon is inflated or with the infusion of the sterile saline solution. The majority of the patients tell us that this is a very easy and painless procedure. Unfortunately, there are potential complications of all medical procedures. Fortunately, a sonohysterogram is considered a very safe procedure. Since diagnostic ultrasound uses only sound waves, no harmful effects are currently known. A rare complication of any procedure which involves infusion of fluid into the uterus is infection of the uterus, tubes, and ovaries.

6.   Describe any risks related to the use of radioisotopes/radiation-producing machines (e.g., X-rays, CT scans, fluoroscopy).

7.   Describe why this investigational compound/drug/device/procedure's risks/benefits are potentially better than standard of care or other common alternatives. Any standard treatment that is being withheld must be disclosed and the information must be included in the consent form. *?HELP?*

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Alternatively, the subject may decline the sonohysterogram. Unable to view the healing process of the uterine wall without the procedure. Sonohysterogram is available outside of this study and could be preformed by a private physician. No standard treatment or procedure is being withheld.

8.   **Describe any psychological, social, or legal risks the subject may experience. *?HELP?***

•Some questions may make you feel uncomfortable. You may choose not to answer any question with which you feel uncomfortable.
•Every effort will be made to protect your research study data. There is, however, always the possibility of a breach of confidentiality.

Page numbers from a sponsor's protocol/grant may be referenced in 9.9 and 9.10.

9.   **Special Precautions. Describe the planned procedures for protecting against or minimizing potential risks. If appropriate, include the standards for termination of the participation of the individual subject. Discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects.**

Procedures to maintain confidentiality
Password access
Coded, with a master list kept as a hardcopy or on a secure network (confidential)
Secure network
Locke suite
Locked office

If a subject is found to be pregnant at the time of the sonohysterogram, the subject will be excluded from the study.

10.   **Reproductive Risks.**

a.   **Please list the pregnancy category of any drugs or N/A.**

N/A

   Please describe any reproductive risk associated with any part of the research study. Include any data from other studies (animal or human).

Protocol Title: Evaluation of Hysterotomy Site after Open Fetal Surgery

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This procedure evaluates the healing process of the uterine wall after the mother has had open fetal surgery. Information needed for future pregnancies.

If using an IUD (intrauterine device)to prevent pregnancy the sonohysterogram will not be completed.

Should a woman be pregnant during the performance of a sonohysteorgram, the risks include no harm, potential bleeding and miscarriage. If a subject is found to be pregnant at the time of the sonohysterogram, the subject will be excluded from the study.

NB: a pregnancy test will be done prior to the performance and an ultrasound prior to performance. In this way, three methods have been utilized to assure non-pregnancy: patient interview, urine pregnancy test and ultrasound.

       11. **Data Safety Monitoring**

Federal regulations require that when appropriate, the research protocol makes adequate provisions for monitoring the data to ensure the safety of participants. Monitoring should be commensurate with risks and with the size and complexity of the research, and could range from no plan needed to an independent data safety monitoring board. Please refer to <a href=http://www.slu.edu/Documents/research/IRB/Data_Safety_Monitoring.doc target=_blank > SLU Guidelines for Data and Safety Monitoring as you complete the questions below.

a. Is there a Data Monitoring Committee (DMC) or Board (DSMB)? N/A

If yes, please provide the following information (labeled a-g): a) the composition of the board (degrees/qualifications of members), b) whether the board is independent from the sponsor and research team or not, c) frequency of meetings and issuance of reports to sites, d) assurance that the board is reviewing aggregate safety data and making recommendations regarding study continuance, e) provisions for ad hoc meetings if needed, f) who is reviewing SAEs in real time (MD or DO), and g) stopping/halting rules (if any exist).
A DSM charter can be referenced for all items except for "f) who is reviewing SAEs in real time."

If no, please justify why not.

         Is there a Data Safety Monitoring Plan (DSMP)? N/A

bsp
&nb
sp&
nbs
pb.

Note, if all relevant plan information is included in DSMB question above, select 'Yes' and state "see above" in the answer box.

If yes, provide details (labeled a-e) including: a) what types of data or events are captured and how are they documented, b) who is monitoring data, their independence/affiliation with the research and their degrees/qualifications, c) frequency of aggregate data review, d) who is reviewing SAEs in real time (MD or DO), and e) stopping/halting rules (if any exist).

If no, please justify why not.

12.   In case of international research (research outside of the U.S. or research on international populations (non-U.S.)), describe qualifications/preparations that enable you to evaluate cultural appropriateness and estimate/minimize risks to subjects. Include whether research is sensitive given cultural norms.

a.   State any local laws/regulations governing Human Subjects Research in the country(ies) you will conduct the research and attach any relevant approvals. If none, state N/A.

b.   Will there be language barriers and if so, how will they be addressed?
Note: If materials are to be distributed to subjects in their native language, please follow SLU's Guidance For Studies Involving Non-English Speaking Subjects.

          NOTE: Export control laws include the transfer of technical information and data, as well as information   and technology to foreign nationals. If this study has international components, contact the <a href=http://www.slu.edu/general-counsel-home/compliance/export-controls target=_blank > SLU Export   <a href=http://www.slu.edu/general-counsel-home/compliance/export-controls target=_blank >Control Officer for direction on whether export control policies apply.

Protocol Title: Evaluation of Hysterotomy Site after Open Fetal Surgery

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* * * Benefits/Alternatives, Procedures to Maintain Confidentiality and Privacy * * *

10. Benefits/Alternatives

a) **Benefits. Describe the potential benefit(s) to be gained by the subjects and how the results of the study may benefit future subjects and/or society in general. Indicate if there is no direct benefit to the participants.**

Better understand the health of her uterus and potential for future pregnancies.
The information shared will be the depth and characteristics of the uterine scar from the open fetal surgery hysterotomy (parenthetically, the cesarean section hysterotomy will also be seen, evaluated). Should this layer be extremely thin, recommendations regarding future pregnancies will be shared.

Early data regarding hysterotomy at cesarean section (low transverse cesarean section) has revealed a uterine wall thickness < 1.2 mm has an increased association with uterine rupture. There is no data, at this time, with respect to the hysterotomy created at open fetal surgery: non-low transverse hysterotomy. Hence, if this data also correlates with future uterine compromise/risks, this can be shared with a woman who has undergone the sonohystergram. She/society would then understand the increased risk at a future pregnancy: both to the patient and the unborn.

b) **Alternatives. Describe any alternative treatments and procedures available to the subjects should they choose not to participate in the study. If no such alternatives exist, please state that the alternative is nonparticipation. For some studies, such as record reviews, a description of alternatives would not be applicable.**

The alternative would be non-participation.
Mothers have access to sonohysterography outside of this protocol if their physician determines that they would benefit from the test.

Stand of care (SOC) after open fetal surgery is, at this time, no different than that of a cesarean delivery: physician visits at 1 - 2 weeks postpartum and at 6 weeks (the close of the purpureum).

11. Procedures to Maintain Confidentiality and Privacy

Federal regulations require that research materials be kept for a minimum of three (3) years and HIPAA documents be kept for a minimum of six (6) years after the closure of the study. For FDA-regulated or sponsored projects, the PI may be required to keep the data and documents for a longer time period.

Confidentiality

To determine whether adequate provisions for confidentiality of data are in place, the IRB must ensure that research materials are stored in appropriate locations throughout the study (during collection, transport/transmission, analysis and long term storage). Research information must be protected using appropriate safeguards based on identifiability of the data and risk associated with the study (See SLU IRB Confidentiality Guidelines).

For the questions below, please use the following definitions:

**   Anonymous/De-identified: data contain no identifiers, including code numbers that investigators can link to   individual identities;**

**   Coded: data in which (1) identifying information, such as name or social security number, has been replaced   with a number, letter, symbol, or combination thereof (i.e., the code), and (2) a key to decipher the code exists**

     enabling linkage of data to identifying information (e.g., a master list), and (3) the key (master list) is kept   separately from coded data; AND/OR

     Identifiable: data that includes personal identifiers (e.g., name, social security number), such that information   could be readily connected to respective individuals.

a)&n Electronic (Computer) Data
bsp

Click "Add" to enter data security information for each type of electronic data that will be created in the study: anonymous/de-identified, coded, and/or identifiable (see definitions above).

To properly address this question, there should only be one listing of each type of data in the table. Depending on your project, you could have up to three types of data. See the SLU ITS Sensitive Data Guide for acceptable data security methods.

Not Applicable, No Electronic (Computer) Data

Study IRB-approved Prior to New Question (Question N/A- Grandfathered)

Electronic Data

Type of Data	Storage Location	Data Transmission Outside of SLU	Supplemental information related to above items can be entered here or leave blank:
Coded	SLU ITS managed device (computer, tablet, etc.) with encryption; Collection or Storage of data in SLU REDCap	Use of SLU REDCap account; Use of an external Secure Web Mail account	SSM ITS managed device with encryption

b) Hardcopy (Paper) Data

Click "Add" to enter information for each type of hardcopy (paper) data that will be created in the study: anonymous/de-identified, coded, and/or identifiable (see definitions above).

To properly address this question, there should only be one listing of each type of data in the table. Depending on your project, you could have up to three types of data.

Not Applicable, No Hardcopy (Paper) Data

X Study IRB-approved Prior to New Question (Question N/A- Grandfathered)

c) If a master list is used in this study (linking study codes to subject identifiers), explain: a) how and where you will secure the master list, b) how long it will be kept/when it will be destroyed, and c) provide a sample of the code.

Code numbers are used to link patients to their data. Code and identifiers will be kept separate.
Dates will not be used.
Post op days will be calculated at the time data is abstracted
Gestational age will be noted in weeks and days
Birth dates will not be noted. Mothers age will be noted at time of open fetal surgery

d) If data or specimens are being shared outside of the research team, indicate who will receive the material and specifically what they will receive (data or specimens).

De-identified information will be shared with Dr. Emanuel (Mike) Vlastos, former PI, as needed for data analysis and manuscript publication.

e) If samples or data will be provided from an outside source, indicate whether you will have access to identifiers, and if so, how identifiable information is protected.

n/a

f) If data will be collected via e-mail or the Internet, how will anonymity or confidentiality be affected? Describe how data will be recorded (i.e., will internet protocol (IP) addresses and/or e-mail addresses be removed from data?).

g) If you will be audio/video recording or photographing subjects, provide a rationale as voiceprints and images of faces/unique body markings are considered identifiers. Describe confidentiality procedures, including any restricted access to images and/or the final disposition of the recordings/photos (destruction, archiving, etc.).

The sonohysterogram will be analyzed per protocol and data added to datasheet as per protocol. The sonohysterogram reports will be archived in mother's chart. Confidentiality will be maintained according to HIPAA protocols.

h) Describe any study-specific (non standard of care) information or documentation that will be put in the participants' medical records for this research (e.g., study visit notes, lab results, etc.). If none, state "not applicable".

n/a

i) Are there any information security requirements identified in the project's RFP/Award Notice/Contract? This could include data security, technical safeguards, security controls, NIST, FISMA, CFR, etc. N

If yes, SLU ITS approval is required. Contact InfoSecurityTeam@slu.edu to start the approval process.

Privacy

Privacy refers to persons having control over the sharing of oneself with others.

  j)   Please indicate how participant privacy will be protected in this study (select all that apply):

X Discussion of health related and/or personal information in a private room/area

X Research interactions/interventions are conducted in a private room/area

X Use of drapes or other privacy measures

X Collection of sensitive/identifiable information is limited to the minimum necessary to achieve the aims of the research

X Access to study information is limited to the minimum amount of persons necessary to achieve the aims of the research (e.g., access restricted to research team members only)

Consideration of parental inclusion/absence for studies involving minors

Other (please explain):

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* * * Potential Conflict of Interest * * *

12. Potential Conflict of Interest

Indicate whether you, your spouse or dependent children, have, or anticipate having, any income from or financial interest in a sponsor, device or drug manufacturer of this protocol, or a company that owns/licenses the technology being studied. Please remember that you are responding for you and any other investigator participating in the study. Financial Interest includes but is not limited to: consulting; speaking or other fees; honoraria; gifts; licensing revenues; equity interests (including stock, stock options, warrants, partnership and other equitable ownership interests). For questions regarding Conflict of Interest consult the Conflict of Interest in Research Policy.

Check one of the following (please remember that you are responding for yourself, your spouse, dependent children and any investigator, investigator's spouse and dependent children participating in the study):

1) X No equity interest and/or Financial Interest less than or equal to $5K
2) Any equity interest and/or Financial Interest exceeding $5K but not exceeding $25K in the past year or expected in the current year
3) Financial Interest exceeding $25K in the past year or expected in the current year

Protocol Title: Evaluation of Hysterotomy Site after Open Fetal Surgery

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Check all those that apply:

Consulting
Speaking Fees or Honoraria
Gifts
Licensing agreement or royalty income
Equity interests, (including stock, stock options, warrants, partnership or equitable ownership interests), or serving on a scientific advisory board or board of directors
Other fees/compensation

If you have marked #2 or #3, please contact coi@slu.edu to initiate review of this study and provide the following information:

1. A Conflict of Interest Management Plan.
   has been approved for all investigators for this study
   is pending
   has not been initiated

2. Describe who has, and briefly explain, the conflict of interest and indicate specific amounts for each subcategory checked:

Note to Investigator(s) Reporting a Potential Conflict of Interest

Investigator(s) must have:

1. Current, up-to-date Conflict of Interest Disclosure Form on file with the SLU Conflict of Interest in Research Committee (COIRC) that describes any financial relationship indicated above.

   . This information must be disclosed on the SLU confidential Conflict of Interest Disclosure Form and reviewed by the COIRC before accruing research subjects in this study. If your current Disclosure Form does not contain this information, you are required to submit an updated Disclosure Form to the COIRC.

2. You may not begin your study until your disclosure form has been reviewed and any required management plan has been approved by the COIRC for this study. To initiate COIRC review of your study, please contact coi@slu.edu.

*** * * Informed Consent * * ***

13. Informed Consent

Federal regulations require that informed consent be obtained from individuals prior to their participation in research unless the IRB grants a waiver of consent. Answer the questions, below, then click Add to provide the necessary consent documents and information regarding subject consent. Multiple consents/waivers may be added, but they must be uploaded one at a time.

NOTE: You may refer to the SLU IRB Guidance for Obtaining Informed Consent for considerations regarding the consent/assent process.

State N/A if not applicable.

1) How is consent being obtained? When and where will the discussion take place? If the study involves a non-English Speaking participant/population, please include details about plans for translated materials and interpreters to be used (see <a href=https://www.slu.edu/Documents/research/IRB/Non-English_Speaking_Subjects.doc target=_blank>SLU Guidelines for Involving Non-English Speaking Subjects for more details).

Retrospectively, consent will be obtained by phone contact from a member of the research team, the study will be described and they will be asked if they are interested in participating. All questions will be answered. The consent, HIPAA authorization, and Notice of Privacy Practices will be mailed to them
with highlighted areas needing to be signed. An addressed return envelope will be included for their convenience when returning the signed information to the FCI. When the consent is returned it will be
dated, signed, copied and the copy will be mailed to the mother.

Prospectively, the subject will be consented in clinic after she has decided to have open fetal surgery. If time does not allow for consent prior to surgery, consent will be completed at a follow-up appointment. A member of the research team will consent for the study, give a Notice of Privacy Practices, and the obtain the HIPAA authorization. A signed copy of the consent, HIPAA authorization and Notice of Privacy Practices will be given to the subject. Mothers will be directed to the PI if there are any questions or concerns regarding this research study.

Retrospectively, mothers who have previously consented for this study and informed of the change in protocol by phone will be asked if there were any questions. A verbal consent will be requested and read back for the waiver of consent for this subgroup of the protocol and documented in the research record.

2) If the study involves adults unable to consent for themselves (whether diminished capacity to consent is temporary, permanent, progressive or fluctuating), please address the following: a) how is capacity to provide consent being assessed (initially and throughout study, if applicable); b) if unable to provide consent, how is LAR being determined (See <a href=https://www.slu.edu/Documents/research/IRB/LAR_Guidelines.docx target=_blank>SLU LAR Guidelines); c) if unable to provide consent, will assent be obtained and if not, why not?; d) if unable to provide assent, will dissent be honored and if not, why not? Note: participants initially unable to provide consent for themselves are expected to be given an opportunity to provide consent once capacity is gained. See <a href=https://www.slu.edu/Documents/research/IRB/Adults_Unable_to_Provide_Consent.docx target=_blank>SLU Guidelines for Adults Unable to Provide Consent for additional detail.

n/a

Note: Any assent documents which will be used per the Adults Unable to Provide Consent guidance, should be appropriately named and uploaded using the Add button and the Consent drop down menu

selection.

Informed Consent

Title	Consent Type	Attached Date
Waiver 22581	Waiver of Written Consent	
Approved_22581 consent version 8	Consent	05/05/2017

* * * Assent * * *

14. Assent

Complete this section if your study includes minors. The Assent Form Template provides guidelines for writing assent documents.

1. Will minors be asked to give assent, then consent once they reach adulthood? If not, please justify. If not capable to provide assent initially, please address whether assent will be obtained as the minor gains capacity. Note: children who reach the age of adulthood during participation should be given the opportunity to provide consent as parent/guardian consent no longer applies. If obtaining consent would be impracticable (e.g., this is a registry with data/specimen obtained long ago), a waiver of consent should be added for IRB review. See <a href=https://www.slu.edu/Documents/research/IRB/Minors_in_Research.doc target=_blank>SLU Guidelines for Research Involving Minors for additional detail.

   Mothers' infants are to young to require assent.

2. If minors are asked to assent and do not wish to participate, will they still be accrued in the study? If yes, justify.

   n/a

3. How will the minor's ability to give assent be assessed? (Consider the age and maturity of the minors as well as their physical or mental condition). If capacity is fluctuating, please explain how capacity will be assessed throughout the study.

   n/a

Note: For studies that require a discussion about reproductive risks, note that the conversation with the minor should take place separately from the parents. Also, if a minor will reach adulthood (18 in Missouri) during the course of the study, they will need to be asked to consent as an adult at that time to continue in the study.

* * * HIPAA * * *

15. HIPAA

Studies that access, receive or collect protected health information (PHI) are subject to HIPAA regulations. PHI is health information with one or more personal identifiers. For more information visit the IRB HIPAA page or refer to the SLU IRB HIPAA Guidance.

1. Will health information be accessed, received or collected?

No health information. HIPAA does not apply.

X Yes (continue to question 2).

2. Which personal identifiers will be received or collected/recorded?

No identifiers. I certify that no identifiers from the list below will be received or collected and linked to health information. (Skip remainder of page).

Limited identifiers will be received or collected/recorded (study will likely require a data use agreement). Select Data Use Agreement- INTERNAL or Data Use Agreement- EXTERNAL as appropriate, below.

City/State/Zip codes

Person-specific dates (e.g., date of birth, dates of service, admission/discharge dates, etc.)

Age (if subjects are 90+ years)

At least one direct identifier will be received or collected/recorded.

X Names

Social Security numbers

X Telephone numbers

X Linkable code or any other unique identifying number (note this does not mean the unique code assigned by the Investigator(s) to code the research data)

X All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if, according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000

X All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older

Fax numbers

X Electronic mail addresses

Medical record numbers

Health plan beneficiary numbers

Account numbers

Certificate/license numbers

Vehicle identifiers and serial numbers, including license plate numbers

Device identifiers and serial numbers

Web Universal Resource Locations (URLs)

Internet Protocol (IP) address numbers

Biometric identifiers, including finger and voice prints
Full face photographic images and any comparable images

If you are receiving or collecting/recording health information and at least one personal identifier, please continue to complete the sections, below.

3. Sources of Protected Health Information:

- X Hospital/medical records for in or out patients
- X Physician/clinic records
- Laboratory, pathology and/or radiology results
- Biological samples
- X Interviews or questionnaires/health histories
- Mental health records
- Data previously collected for research purposes
- Billing records
- X Other

Please describe:

Sonohysterogram

4. If data will be shared outside the research team and the study involves PHI indicate how the research team will share the information.

- X Not applicable (continue to question 5).
- Only linkable code that can link data to the identity of the subject. A code access agreement or business associate agreement may be needed when data are shared with other non-SLU entities. If necessary, the agreement can be added and uploaded in item #5, below.
- Limited identifiers: Zip codes, dates of birth, or other dates only. The study qualifies as a Limited Data Set. A data use agreement may be needed when data are shared with other non-SLU entities. If necessary, the agreement can be added and uploaded in item #5, below, using DUA-external option.
- With unlimited identifiers. The consent document and HIPAA Authorization form must describe how the information will be disclosed.

5. HIPAA Documentation is required for this study. Use the table below to add HIPAA Documents for your study.

HIPAA Documents

HIPAA Documents	Title	Attached Date
HIPAA Authorization	Approved_22581_HIPAA_Version_2	03/25/2013

Protocol Title: Evaluation of Hysterotomy Site after Open Fetal Surgery

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* * * Event History * * *

Event History

Date	Status	View Attachments	Letters
12/20/2017	CLOSED		
12/20/2017	FINAL FORM APPROVED	Y	Y
12/20/2017	FINAL FORM REVIEWER(S) ASSIGNED		
12/19/2017	FINAL FORM SUBMITTED	Y	
12/19/2017	FINAL FORM CREATED		
06/30/2017	AMENDMENT 8 FORM APPROVED	Y	Y
06/30/2017	AMENDMENT 8 FORM REVIEWER(S) ASSIGNED		
06/26/2017	AMENDMENT 8 FORM SUBMITTED (CYCLE 1)	Y	
06/23/2017	AMENDMENT 8 FORM PANEL MANAGER REVIEW		
06/15/2017	AMENDMENT 8 FORM SUBMITTED	Y	
05/24/2017	AMENDMENT 8 FORM CREATED		
05/05/2017	AMENDMENT 7 FORM APPROVED	Y	Y
05/04/2017	AMENDMENT 7 FORM REVIEWER(S) ASSIGNED		
04/26/2017	AMENDMENT 7 FORM SUBMITTED (CYCLE 1)	Y	
04/21/2017	AMENDMENT 7 FORM PANEL MANAGER REVIEW		
04/17/2017	AMENDMENT 7 FORM PANEL REASSIGNED		
04/17/2017	AMENDMENT 7 FORM SUBMITTED	Y	
04/13/2017	AMENDMENT 7 FORM CREATED		
01/20/2017	CONTINUING REVIEW 4 FORM APPROVED	Y	Y
01/06/2017	CONTINUING REVIEW 4 FORM REVIEWER(S) ASSIGNED		

01/06/2017	CONTINUING REVIEW 4 FORM PANEL MANAGER REVIEW		
01/03/2017	CONTINUING REVIEW 4 FORM PANEL REASSIGNED		
12/28/2016	CONTINUING REVIEW 4 FORM SUBMITTED	Y	
12/06/2016	CONTINUING REVIEW 4 FORM CREATED		
08/25/2016	AMENDMENT 6 FORM APPROVED	Y	Y
08/25/2016	AMENDMENT 6 FORM REVIEWER(S) ASSIGNED		
08/25/2016	AMENDMENT 6 FORM SUBMITTED (CYCLE 1)	Y	
08/25/2016	AMENDMENT 6 FORM PANEL MANAGER REVIEW		
08/25/2016	AMENDMENT 6 FORM PANEL MANAGER REVIEW		
08/22/2016	AMENDMENT 6 FORM SUBMITTED	Y	
08/11/2016	AMENDMENT 6 FORM CREATED		
03/03/2016	AMENDMENT 5 FORM APPROVED	Y	Y
03/02/2016	AMENDMENT 5 FORM REVIEWER(S) ASSIGNED		
02/29/2016	AMENDMENT 5 FORM PANEL REASSIGNED		
02/29/2016	AMENDMENT 5 FORM SUBMITTED	Y	
02/29/2016	AMENDMENT 5 FORM CREATED		
02/10/2016	CONTINUING REVIEW 3 FORM APPROVED	Y	Y
02/10/2016	CONTINUING REVIEW 3 FORM REVIEWER(S) ASSIGNED		
02/05/2016	PROTOCOL EXPIRED	Y	
02/02/2016	CONTINUING REVIEW 3 FORM CONTINGENT		
01/22/2016	CONTINUING REVIEW 3 FORM REVIEWER(S) ASSIGNED		
01/22/2016	CONTINUING REVIEW 3 FORM PANEL MANAGER REVIEW		
01/08/2016	CONTINUING REVIEW 3 FORM PANEL REASSIGNED		

01/07/2016	CONTINUING REVIEW 3 FORM SUBMITTED	Y	
12/07/2015	CONTINUING REVIEW 3 FORM CREATED		
06/04/2015	AMENDMENT 4 FORM APPROVED	Y	Y
06/03/2015	AMENDMENT 4 FORM REVIEWER(S) ASSIGNED		
06/02/2015	AMENDMENT 4 FORM PANEL REASSIGNED		
06/01/2015	AMENDMENT 4 FORM SUBMITTED	Y	
05/29/2015	AMENDMENT 4 FORM CREATED		
01/08/2015	CONTINUING REVIEW 2 FORM APPROVED	Y	Y
12/19/2014	CONTINUING REVIEW 2 FORM REVIEWER(S) ASSIGNED		
12/17/2014	CONTINUING REVIEW 2 FORM PANEL MANAGER REVIEW		
12/15/2014	CONTINUING REVIEW 2 FORM PANEL REASSIGNED		
12/15/2014	CONTINUING REVIEW 2 FORM PANEL REASSIGNED		
12/15/2014	CONTINUING REVIEW 2 FORM SUBMITTED	Y	
12/09/2014	CONTINUING REVIEW 2 FORM CREATED		
07/28/2014	AMENDMENT 3 FORM APPROVED	Y	Y
07/25/2014	AMENDMENT 3 FORM REVIEWER(S) ASSIGNED		
07/24/2014	AMENDMENT 3 FORM PANEL REASSIGNED		
07/21/2014	AMENDMENT 3 FORM SUBMITTED	Y	
07/21/2014	AMENDMENT 3 FORM CREATED		
02/05/2014	CONTINUING REVIEW 1 FORM APPROVED	Y	Y
02/05/2014	PROTOCOL EXPIRED		
01/24/2014	CONTINUING REVIEW 1 FORM REVIEWER(S) ASSIGNED		
01/22/2014	CONTINUING REVIEW 1 FORM PANEL MANAGER REVIEW		

01/22/2014	CONTINUING REVIEW 1 FORM PANEL REASSIGNED		
01/09/2014	CONTINUING REVIEW 1 FORM RESUBMITTED	Y	
12/20/2013	CONTINUING REVIEW 1 FORM RETURNED		
12/16/2013	CONTINUING REVIEW 1 FORM SUBMITTED	Y	
12/09/2013	CONTINUING REVIEW 1 FORM CREATED		
10/11/2013	AMENDMENT 2 FORM APPROVED	Y	Y
10/09/2013	AMENDMENT 2 FORM REVIEWER(S) ASSIGNED		
10/08/2013	AMENDMENT 2 FORM SUBMITTED (CYCLE 2)	Y	
09/24/2013	AMENDMENT 2 FORM SUBMITTED (CYCLE 1)	Y	
09/19/2013	AMENDMENT 2 FORM CONTINGENT		
09/06/2013	AMENDMENT 2 FORM REVIEWER(S) ASSIGNED		
09/06/2013	AMENDMENT 2 FORM PANEL REASSIGNED		
09/06/2013	AMENDMENT 2 FORM REVIEWER(S) ASSIGNED		
09/03/2013	AMENDMENT 2 FORM RESUBMITTED	Y	
08/29/2013	AMENDMENT 2 FORM RETURNED		
08/27/2013	AMENDMENT 2 FORM SUBMITTED	Y	
08/15/2013	AMENDMENT 2 FORM CREATED		
07/15/2013	REPORT 1 FORM DELETED		
07/05/2013	AMENDMENT 1 FORM APPROVED	Y	Y
07/05/2013	AMENDMENT 1 FORM REVIEWER(S) ASSIGNED		
07/01/2013	AMENDMENT 1 FORM PANEL REASSIGNED		
07/01/2013	AMENDMENT 1 FORM PANEL REASSIGNED		
07/01/2013	AMENDMENT 1 FORM SUBMITTED	Y	
06/20/2013	REPORT 1 FORM CREATED		
06/07/2013	AMENDMENT 1 FORM CREATED		

Protocol Title: Evaluation of Hysterotomy Site after Open Fetal Surgery

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03/26/2013	NEW FORM APPROVED	Y	Y
03/25/2013	NEW FORM REVIEWER(S) ASSIGNED		
02/07/2013	NEW FORM CONTINGENT		
01/25/2013	NEW FORM REVIEWER(S) ASSIGNED		
01/09/2013	NEW FORM PANEL MANAGER REVIEW		
01/07/2013	NEW FORM PANEL REASSIGNED		
01/07/2013	NEW FORM PANEL ASSIGNED		
01/04/2013	NEW FORM SUBMITTED	Y	
01/04/2013	NEW FORM PREREVIEWED		
01/03/2013	NEW FORM PREAPPROVAL		
09/10/2012	NEW FORM CREATED		