

Protocol Title:	Safety and Efficacy of Sonohysterosalpingography for the Evaluation of Infertility
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IRB Number:	

Guidelines for Preparing a Research Protocol

Instructions:

- You do not need to complete this document if you are submitting an *Application for Exemption* or *Application for a Chart Review*.
- Do not use this template if:
 - Your study involves an FDA regulated product. In this case, use the *Clinical Trial Protocol Template*.
 - Your study has a protocol from a sponsor or cooperative group. In this case, use the *Protocol Plus*.
 - Your study is a registry or repository for data and/or samples, In this case, use *Protocol Template – Registry Studies*.
- If a section of this protocol is not applicable, please indicate such.
- Do not delete any of the text contained within this document.
- Please make sure to keep an electronic copy of this document. You will need to use it, if you make modifications in the future.
- Start by entering study information into the table above, according to these rules:
 - Protocol Title: Include the full protocol title as listed on the application.
 - Investigator: include the principal investigator’s name as listed on the application form
 - IRB Number: Indicate the assigned IRB number, when known. At initial submission, this row will be left blank.
- Once the table information in entered, proceed to page 2 and complete the rest of the form.

↓ Continue to next page to begin entering information about this study ↓

1. PREVIOUS STUDY HISTORY

Has this study ever been reviewed and rejected/disapproved by another IRB prior to submission to this IRB?

No Yes – if yes, please explain:

2. BRIEF SUMMARY OF RESEARCH

- *The summary should be written in language intelligible to a moderately educated, non-scientific layperson.*
- *It should contain a clear statement of the rationale and hypothesis of your study, a concise description of the methodology, with an emphasis on what will happen to the subjects, and a discussion of the results.*
- *This section should be ½ page*

This pilot study is a collaborative effort between Northwell Health Fertility and the Radiology Department to streamline the fertility evaluation process and reduce the burden of stress many fertility patients experience by eliminating an imaging examination which is painful and exposes the patient to potentially harmful radiation.

The aim of this study is to improve the workup of infertility by integrating the examination of structural abnormalities of the fallopian tubes and uterus into a single radiation-free ultrasound guided procedure, the sonohysterosalpingogram (sonoHSG). Confirmation of tubal patency is extremely important as approximately 25-35% of female infertility can be attributed to fallopian tube pathology.¹ The current paradigm is to use two separate imaging exams; the hysterosalpingogram (HSG), a transvaginal procedure that uses radiation and iodinated contrast to visualize the fallopian tubes, and the sonohysterogram, a transvaginal procedure that uses ultrasound and saline to visualize the uterus. By using agitated saline, to produce air bubbles, fallopian tube visualization is optimized during the time of sonohysterogram (sonoHSG). We plan to also utilize a continuous saline-air device that may produce a technically superior sonoHSG.

As a result of this study, the Radiology Department and Northwell Health Fertility will work together to encourage, educate, and support physicians to promote the utility of sonoHSG as the first imaging examination for the infertility workup.

Currently, our institution is not routinely utilizing the sonoHSG despite the advantages in safety, comfort, and convenience to the patient. We aim to effect a change in the current practice at our institution by increasing the knowledge and visibility of the sonoHSG by creating educational materials for referring physicians, and creating a pilot program that demonstrates the value and efficacy of the exam. SonoHSG can be performed concurrently at the time of the sonohysterogram at no additional cost to the patient.

We will enroll 30 patients from Northwell Health Fertility over the course of one

year. Measures of success will include concordance between sonoHSG and HSG in patients who receive both procedures, and patient surveys evaluating pain utilizing the pain scale. If sonoHSG proves to be efficacious, our future steps will be to educate referring physicians and patients about the utility of the examination using print materials and a grand rounds lecture. We will also measure the number of sonoHSGs ordered compared to HSGs for the evaluation of fallopian tube patency in order to evaluate if there has been a shift in the standard of care.

3. INTRODUCTION/BACKGROUND MATERIAL/PRELIMINARY STUDIES AND SIGNIFICANCE

- *Describe and provide the results of previous work by yourself or others, including animal studies, laboratory studies, pilot studies, pre-clinical and/or clinical studies involving the compound or device to be studied.*
- *Include information as to why you are conducting the study and how the study differs from what has been previously researched, including what the knowledge gaps are.*
- *Describe the importance of the knowledge expected to result*

Recently, studies have shown that the sonoHSG alone is as reliable as the traditional HSG for evaluating fallopian tube patency, with the benefits of eliminating radiation exposure and the use of potentially harmful iodinated contrast.^{2,3} SonoHSG is also less painful when compared to the HSG^{4,9} and by reducing the number of procedures from two to one, the risk of infection is reduced. Additionally, a single procedure will help to shorten the diagnostic process of infertility and expedite treatment. Indeed, several recent reports support the use of sonoHSG as a first line diagnostic test for the workup of infertility.^{5,6} Ultimately, this test will be safer, more comfortable, and less expensive for our patients. SonoHSG is a long sought for alternative for tubal patency in place of the old, yet still practiced, “gold standard” HSG. We believe this initiative will help our institution streamline time to treatment and diagnosis of tubal pathology while improving patient experience.

The results of the study will be significant in determining and possibly changing the standard of care procedure from HSG to sonoHSG. Currently, the first line examination for the evaluation of fallopian tube patency is the hysterosalpingogram (HSG). This test involves radiation exposure, the use of iodinated contrast, and is accompanied by significant patient discomfort secondary to painful cervical manipulation and at times violent uterine contractions.⁴ Some patients also require a sonohysterogram (aka a “water ultrasound”) to better evaluate the endometrial lining and to assess for polyps, scar tissue, fibroids, or congenital uterine anomalies that may prevent a successful pregnancy. This initiative will extend the diagnostic capacity of the sonohysterogram by utilizing air bubbles, via a continuous air saline device, to allow concurrent visualization of the fallopian tubes (sonohysterosalpingography). Prior studies have shown, and our experience confirms, that fallopian tube patency can be accurately confirmed by sonoHSG and results are concordant with the HSG.³

The Radiology Department and Northwell Health Fertility will work together to encourage, educate, and support physicians to promote the utility of sonoHSG as the first imaging examination for the infertility workup. Currently, our institution is not routinely utilizing sonoHSG despite the advantages in safety, comfort, and convenience to the patient. We aim to effect a change in the current practice at our institution by increasing the knowledge and visibility of the sonoHSG by creating educational materials for referring physicians, and

creating a pilot program that demonstrates the value and efficacy of the exam. SonoHSG can be performed concurrently at the time of sonohysterogram at no additional cost to the patient.

4. OBJECTIVE(S)/SPECIFIC AIMS AND HYPOTHESES

- *A concise statement of the goal(s) of the current study.*
- *The rationale for and specific objectives of the study.*
- *The goals and the hypothesis to be tested should be stated.*

The specific aim of this study is to evaluate the feasibility of the sonoHSG for it to be determined as the standard of care. Additionally, this is to improve the workup of infertility by integrating the examination of structural abnormalities of the fallopian tubes and uterus into a single radiation-free ultrasound guided procedure, the *sonohysterosalpingogram*.

The specific goals are:

- To demonstrate the utility of sonoHSG as a first line imaging examination in the workup of infertility.
- To streamline the workup of infertility by diagnosing tubal pathology at the time of sonohysterogram.
- To make the workup of infertility safer.
- To improve patient comfort.
- To assess the side effects and complications of and difficulties related to the procedure.
- To assess patient tolerance by using the Pain Scale.

5. RESOURCES AVAILABLE TO CONDUCT THE HUMAN RESEARCH

- *Explain the feasibility of meeting recruitment goals of this project and demonstrate a potential for recruiting the required number of suitable subjects within the agreed recruitment period*
 - *How many potential subjects do you have access to?*
- *Describe your process to ensure that all persons assisting with the trial are adequately informed about the protocol and their trial related duties and functions*

The recruitment goals will be met by enrolling patients from the fertility clinic at the point of care. The accrual goal is 30 participants but we may enroll up to 50 participants. Potentially we have access to 2000 patients.

After IRB approval is obtained, we will have a site initiation meeting to ensure that all study personnel are informed of the process for recruiting subjects, and how the study procedures will be conducted in addition to a detailed review of the study protocol.

6. RECRUITMENT METHODS

- *Describe the source of potential subjects*
- *Describe the methods that will be used to identify potential subjects*
- *Describe any materials that will be used to recruit subjects. A copy of any advertisements (flyers, radio scripts, etc.) should be submitted along with the protocol.*
- *If monetary compensation is to be offered, this should be indicated in the protocol*

We are aiming to recruit 30 patients from the Northwell fertility clinic at the point of care for their infertility work-up. The clinicians in this study will see the potential subjects in their routine clinical care.

The physicians in the Department of Radiology and Northwell Health Fertility will play the dual role of clinician and research investigator.

7. ELIGIBILITY CRITERIA

- *Describe the characteristics of the subject population, including their anticipated number, age, ranges, sex, ethnic background, and health status. Identify the criteria for inclusion or exclusion of any subpopulation.*
- *Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners or other institutionalized individuals, or others who are likely to be vulnerable. You cannot include these populations in your research, unless you indicate such in the protocol*
- *Similarly, detail exclusionary criteria: age limits, special populations (minors, pregnant women, decisionally impaired), use of concomitant medications, subjects with other diseases, severity of illness, etc.*

Inclusion Criteria:

- All women undergoing evaluation for infertility greater than 6 months in the Northwell health system
- Non-pregnant Women Age 18-50
- Diagnosis of male infertility
- Diagnosis of ovulatory dysfunction
- Diminished ovarian reserve, unexplained
- Recurrent pregnancy loss

Exclusion Criteria:

- History of active pelvic infection
- History of tubal ligation or salpingectomy
- History of adverse reaction to iodinated contrast
- Pregnancy

8. NUMBER OF SUBJECTS

- *Indicate the total number of subjects to be accrued locally. If applicable, distinguish between the number of subjects who are expected to be pre-screened, enrolled (consent obtained), randomized and complete the research procedures.*
- *If your study includes different cohorts, include the total number of subjects in each cohort.*
- *If this is multisite study, include total number of subjects across all sites.*

We aim to enroll approximately 30 study subjects. We will go up to enrolling 50 subjects and after this point we will stop enrollment.

Sample Size Justification

The proposed sample size of 30 is based on feasibility, availability of resources, and the study timeline and not on any formal statistical power calculations. Once we have determined the feasibility of the sonoHSG, we intend to proceed with a larger clinical trial and appropriately power that study with a larger sample size.

9. STUDY TIMELINES

- *Describe the duration of an individuals participation in the study*
- *Describe the duration anticipated to enroll all study subjects*
- *The estimated date of study completion*

Study participants will be enrolled in the study for up to 3 weeks.
We anticipate completing enrollment within 12 months.
The estimated time of study completion is 12 months.

10. ENDPOINTS

- *Describe the primary and secondary study endpoints*
- *Describe any primary or secondary safety endpoints*

Primary Study Endpoint:

- Concordance between sonoHSG and HSG results. The sonoHSG and HSG will be considered interchangeable if the level of agreement between them is $\geq 80\%$.

Secondary Endpoint:

- Quantification of level of patient pain in regard to sonoHSG versus HSG

11. RESEARCH PROCEDURES

- *Include a detailed description of all procedures to be performed on the research subject and the schedule for each procedure.*
- *Include any screening procedures for eligibility and/or baseline diagnostic tests*

- *Include procedures being performed to monitor subjects for safety or minimize risks*
- *Include information about drug washout periods*
- *If drugs or biologics are being administered provide information on dosing and route of administration*
- *Clearly indicate which procedures are only being conducted for research purposes.*
- *If any specimens will be used for this research, explain whether they are being collected specifically for research purposes.*
- *Describe any source records that will be used to collect data about subjects*
- *Indicate the data to be collected, including long term follow-up*

Patients will be presented with the study information at the point of contact at the fertility clinic. They will then be contacted via phone prior to their scheduled appointment. A detailed overview of the study will be presented as well as the consent form. Upon verbal agreement over the phone, the clinician and/or study coordinator will go over the consent process in person on the day of the scheduled visit. As part of this study, subjects will have both the HSG and SonoHSG performed consecutively. The HSG will be performed as part of standard of care and the sonoHSG will be performed as part of research. In order to reduce bias, the procedures will be randomized in REDCap before each subject's scheduled visit. The clinicians will be blinded to the results of each procedure until both procedures have been completed.

The pain scale will be administered verbally immediately after each procedure by the technician/other study personnel in the procedure room.

Randomization Scheme

The randomization tables will be set up by the biostatistics department and the randomization model will be set up by a REDCap administrator. The study coordinator will run the randomization in REDCap after the subject has signed their consent form and prior to the initiation of the study procedures. The coordinator will then communicate to the study PI and Co-Investigators the randomization assignment.

Following is the schedule of events that will be followed for each potential subjects:

Schedule of Events:

	Pre-Visit	Visit 1	Follow-Up Visit (1-3 weeks)
Recruit Subject	x	x	
Evaluate Eligibility	x	x	
Initiate Informed Consent	x	x	
Obtain Written Informed Consent		x	
Collect Demographic Information		x	

HSG and sonoHSG (order decided via randomization)		X	
Administer the Pain Scale Survey (following each procedure)		X	
Follow-up with subject via phone to assess any complications/infections			X

The procedures that would account as being research are obtaining informed consent, administering the pain scale surveys, performing the sonoHSG and the follow-up phone call.

Data to be collected and when the data is to be collected

Collection of personal data to avoid duplicating records

The patient’s name, medical record number, age, and health and medical information on diagnoses and medications will be recorded on the Study Eligibility Form to determine eligibility and avoid duplicating records. If the patient meets study eligibility criteria, the patient will be presented with the opportunity of participation in the study. If the patient consents to participate in the study, the subject’s name, medical record number, and assigned Subject ID will be recorded on the Coded Identifier List. The hardcopy Study Eligibility Forms and Coded Identifier List will be stored in a locked file cabinet in the Principal Investigator’s (PI) office with access restricted to the PI and study staff designated by the PI.

Subject ID

A unique Subject ID will be assigned for each enrolled subject and this identifier will follow the subject throughout the course of the study.

Data to be collected/obtained

The Data Collection Form will be completed for each enrolled patient. The data collection form contains the following categories of information to be collected/obtained for each subject:

- Patient record demographic data
- Patient record data on pre-existing co-morbid conditions or underlying disease
- Results of HSG and SonoHSG
- Response to evaluation survey with pain scale

The information that links the subject ID with the PHI (the Coded Identifier List) will be kept in the PI’s locked office and separate from the Data Collection Forms. Coded data from the Data Collection Form will be collected and stored in a REDCap database. The ultrasound images from the sonoHSG will be stored in the research PACS.

12. STATISTICAL ANALYSIS

- *Describe how your data will be used to test the hypotheses.*
- *State clearly what variables will be tested and what statistical tests will be used.*
- *Include sample size calculations.*
- *If this is a pilot study, state which variables will be examined for hypothesis generation in later studies.*

Standard methods for descriptive statistics will be used, such as means, medians, proportions, and their associated 95% confidence intervals.

Concordance of the results between sonoHSG and HSG will be calculated using Gwet's Agreement Coefficient (AC₁). An AC₁ of ≥ 0.80 will be considered successful concordance between the two measures.

A repeated measures analysis of variance (RM-ANOVA) model will be used to examine the effect of treatment (sonoHSG vs. HSG) on the pain measure. The model will include the order in which the treatments are performed and the interaction between order and treatment. If the interaction is not found to be significant, only the main effects of treatment and order will be analyzed.

13. SPECIMEN BANKING

- *If specimens will be banked for future research, describe where the specimens will be stored, how long they will be stored, how they will be accessed and who will have access to the specimens*
- *List the information that will be stored with each specimen, including how specimens are labeled/coded*
- *Describe the procedures to release the specimens, including: the process to request release, approvals required for release, who can obtain the specimens, and the information to be provided with the specimens.*

No specimens will be banked.

14. DATA MANAGEMENT AND CONFIDENTIALITY

- *Describe the data and specimens to be sent out or received. As applicable, describe:*
 - *What information will be included in that data or associated with the specimens?*
 - *Where and how data and specimens will be stored?*
 - *How long the data will be stored?*
 - *Who will have access to the data?*
 - *Who is responsible for receipt or transmission of data and specimens?*

- *Describe the steps that will be taken to secure the data during storage, use and transmission.*

Plan for Data Management:

The PI will be responsible for the collection and storage of study data. The research coordinator will assign and record the Subject IDs on the Coded Identifier List. The hardcopy study eligibility forms and data collection forms will be kept in separate, locked file cabinets in the research office. The data elements from the data collection forms and imaging studies will be recorded in REDCap. The ultrasound images from the sonoHSG will be stored in the research PACS. A research report will be issued and kept as part of the research records. This report will be available to the fertility clinicians to incorporate into their clinical report of the HSG but will not be available in the clinical PACS. Study data in these files will be analyzed by our study statistician(s) on computers that will be protected by passwords and active anti-virus software. Laptops, USB flash drives, and/or external hard drives used for data analysis purposes by our study staff will be protected by password, active anti-virus software, and encryption by Northwell standards. Our data analysts do not have access to the link between the study Subject IDs and patient names.

The PI and Co-Investigators are responsible for ensuring proper study documentation to verify compliance with IRB and GCP guidelines. As part of the safety plan for this study, the study staff will review study patient records to ensure that appropriate mechanisms to protect the safety of study participants are being followed, that protocol requirements are being adhered to, and that data are accurate, complete, and secure. Patient records include consent forms, data collection forms, and/or adverse event logs, and medical charts.

At periodic meetings of the study staff, the PI will report on the number of subjects enrolled in the study.

The coordinator will work with study personnel to securely store and record all study data. Only investigators who are listed on the IRB will have access to PHI associated with the study. All study documents will be stored securely on an IRB and HIPAA compliant system, and paper documents will be stored in a locked office.

15. DATA AND SAFETY MONITORING PLAN

A specific data and safety monitoring plan is only required for greater than minimal risk research. For guidance on creating this plan, please see the [Guidance Document](#) on the HRPP website.

Part I – this part should be completed for all studies that require a DSMP.

Part II – This part should be completed when your study needs a Data and Safety Monitoring Board or Committee (DSMB/C) as part of your Data and Safety Monitoring Plan.

Part I: Elements of the Data and Safety Monitoring Plan

- *Indicate who will perform the data and safety monitoring for this study.*
- *Justify your choice of monitor, in terms of assessed risk to the research subject's health and well being. In studies where the monitor is independent of the study staff, indicate the individual's credentials, relationship to the PI, and rationale for selection*
- *List the specific items that will be monitored for safety (e.g. adverse events, protocol compliance, etc)*
- *Indicate the frequency at which accumulated safety and data information (items listed in # above) will be reviewed by the monitor (s) or the DSMB/C.*
- *Where applicable, describe rules which will guide interruption or alteration of the study design.*
- *Where applicable, indicate dose selection procedures that will be used to minimize toxicity.*
- *Should a temporary or permanent suspension of your study occur, in addition to the IRB, indicate to whom will you report the occurrence.*

The study monitoring will consist of the principal investigator serving as the study's safety monitor. The principal investigator will review the aggregate study data after the first 10 subjects are enrolled and have completed follow-up. The principal investigator will also review the aggregate study data at least annually, starting from the first enrolled subject, until the completion of enrollment and all study follow-up procedures. During these reviews, the principal investigator will review the study data to determine if aspects of the study need to be changed or stopped. In addition, he will review any and all deviations, adverse events and unanticipated problems that may occur to determine their relatedness to the study, their severity, and whether they require study changes. In addition, any unanticipated problems or instances of non-compliance will be reported to the IRB as per their reporting requirements. If any protocol changes are needed, an investigator will submit a modification request to the IRB. Protocol changes will not be implemented prior to IRB approval unless necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB will be promptly informed of the change following implementation.

Part II: Data and Safety Monitoring Board or Committee

- *When appropriate, attach a description of the DSMB.*
- *Provide the number of members and area of professional expertise.*
- *Provide confirmation that the members of the board are all independent of the study.*

No data and safety monitoring board or committee is appointed because the study procedures are standard of care bearing minimum risk.

16. WITHDRAWAL OF SUBJECTS

- *Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent*
- *Describe procedures for orderly termination*

- *Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection.*

The study can be discontinued by the study investigators at any time. Such discontinuation will have no effect on standard patient care.

Subjects can withdraw from the study at any time.

Subjects may be excluded from study analyses due to missing data for one or more of the following reasons:

- Failure to complete both study procedures in the specified time period.
- Failure to complete the pain scale survey.

17. RISKS TO SUBJECTS

- *Describe any potential risks and discomforts to the subject (physical, psychological, social, legal, or other) and assess their likelihood and seriousness and whether side effects are reversible. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.*
- *Include risks to others , like sexual partners (if appropriate)*
- *Discuss why the risks to subjects are reasonable in relation to the anticipated benefits and in relation to the importance of the knowledge that may reasonably be expected to result.*
- *Describe the procedures for protecting against or minimizing any potential risks, including risks to confidentiality, and assess their likely effectiveness.*

Physical Risks:

The study bears minimal risk as ultrasound exams are generally low risk as they are free of radiation. Some risks, although rare, may involve the following:

- Discomfort
- Skin irritation
- Bruising

Risks of the sonoHSG, although rare, may involve the following:

- Infection of the uterus/pelvis
- Bleeding

Psychosocial/Legal Risks:

Several steps have been taken to minimize the loss of confidentiality and privacy with the data collected during this research.

All study records will be organized in files and stored in the PI's locked office. Data will be compiled using a data collection form developed for the study. Results will

also be stored on the PI's computer that is password-protected. Electronic backup files will be stored on a password-protected external drive that will be locked in the PI's office. The research images will be kept in the research PACS. Only the PI and co-investigators will have access to printed and electronic records. If the study results are published, no Protected Health Information (PHI) will be published. The confidentiality of the patient will be preserved under all circumstances.

To minimize the breach of confidentiality risk, we will not use the subject's name or medical record number in any study records. Instead, a unique Subject ID will be assigned to each subject. Only these numbers will be used on study documents that relate to the subject. We will keep the hardcopy Coded Identifier List of subject names and corresponding Subject IDs in a locked file cabinet separate from the hardcopy data collection forms, which are coded only with the Subject ID and also secured in locked storage cabinets in the PI's office.

18. RESEARCH RELATED HARM/INJURY

- *Describe the availability of medical or psychological resources that subjects might need as a result of anticipated problems that may be known to be associated with the research.*
- *If the research is greater than minimal risk, explain any medical treatments that are available if research-related injury occurs, who will provide it, what will be provided, and who will pay for it.*

If the subject is injured as a result of being in the study, they will receive medical care and treatment as needed from Northwell Health. However, the subject will be responsible for the costs of such medical treatment, directly or through their medical insurance or other forms of medical coverage. There is no payment available through the grant or the institution.

19. POTENTIAL BENEFIT TO SUBJECTS

- *Explain what benefits might be derived from participation in the study, noting in particular the benefit over standard treatment (e.g. a once-a-day administration instead of four times a day, an oral formulation over an IV administration).*
- *Also state if there are no known benefits to subjects, but detail the value of knowledge to be gained*

Fertility patients comprise a unique and special group. Women in pursuit of having a child, a family, are often times anxious, nervous and frequently depressed. Navigating the fertility maze may seem cumbersome and overwhelming. This new procedure promises to remove one big, painful hurdle (HSG)⁹ almost every infertile

woman encounters, and allow a happier and faster road to motherhood. This initiative represents major collaboration between Northwell Health Fertility and Radiology and will streamline the diagnosis and treatment of infertility while providing a safer and less painful first line imaging examination for the study participants. The knowledge gained from this study will help to standardize sonohysterosalpingogram in the work up of infertility.

20. PROVISIONS TO PROTECT PRIVACY INTERESTS OF SUBJECTS

- *Describe the methods used to identify potential research subjects, obtain consent and gather information about subjects to ensure that their privacy is not invaded.*
- *In addition consider privacy protections that may be needed due to communications with subjects (such as phone messages or mail).*

Subjects will be identified by clinicians during the course of their routine clinical care. The clinicians may verify eligibility by checking medical record information prior to enrolling the subject.

21. COSTS TO SUBJECTS

- *Describe any foreseeable costs that subjects may incur through participation in the research*
- *Indicate whether research procedures will be billed to insurance or paid for by the research study.*

We do not anticipate that subjects who are participating in this study will have any additional costs to their standard of care procedures. No procedures that are done solely for research purposes will be charged to insurance, and will be charged to the research account.

The HSG will be billed to insurance as it will be performed per standard of care practice. The sonoHSG will be covered for by the Department of Radiology and will not be charged to insurance.

22. PAYMENT TO SUBJECTS

- *Describe the amount of payment to subjects, in what form payment will be received and the timing of the payments.*

No compensation will be provided to the subjects who are participating in this study.

23. CONSENT PROCESS

If obtaining consent for this study, describe:

- *Who will be obtaining consent*
- *Where consent will be obtained*
- *Any waiting period available between informing the prospective participant and obtaining consent*
- *Steps that will be taken to assure the participants' understanding*
- *Any tools that will be utilized during the consent process*
- *Information about how the consent will be documented in writing. If using a standard consent form, indicate such.*
- *Procedures for maintaining informed consent.*

A clinician and/or coordinator on the study will approach the prospective subject at the point of clinical care. If the subject is identified before their visit, study personnel may contact the subject via phone to discuss the protocol. The full written consent process will be done in person on the day of the first visit.

Study personnel will review every element of the consent, giving the subject time to ask questions. If the subject is amenable to enrollment after reviewing the consent, the subject will provide written documentation on the consent form.

In the state of NY, any participants under the age of 18 are considered children. If your study involves children, additional information should be provided to describe:

- *How parental permission will be obtained*
- *From how many parents will parental permission be obtained*
- *Whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. The process used to determine these individual's authority to consent for the child should be provided*
- *Whether or not assent will be obtained from the child*
- *How will assent be documented*
- *Whether child subjects may be expected to attain legal age to consent to the procedures for research prior to the completion of their participation in the research. If so, describe the process that will be used to obtain their legal consent to continue participation in the study. Indicate what will occur if consent is not obtained from the now-adult subjects.*

If the study involves cognitively impaired adults, additional information should be provided to describe:

- *The process to determine whether an individual is capable of consent*
- *Indicate who will make this assessment*

- *The plan should indicate that documentation of the determination and assessment will be placed in the medical record, when applicable, in addition to the research record.*
- *If permission of a legally authorized representative will be obtained,*
 - *list the individuals from who permission will be obtained in order of priority*
 - *Describe the process for assent of subjects; indicate whether assent will be required of all, some or none of the subjects. If some, which subjects will be required to assent and which will not.*
 - *If assent will not be obtained from some or all subjects, provide an explanation as to why not*
 - *Describe whether assent will be documented and the process to document assent*
 - *Indicate if the subject could regain capacity and at what point you would obtain their consent for continued participation in the study*

If the study will enroll non-English speaking subjects:

- *Indicate what language(s) other than English are understood by prospective subjects or representatives*
- *Indicate whether or not consent forms will be translated into a language other than English*
- *Describe the process to ensure that the oral and written information provided to those subjects will be in that language*
- *If non-English speaking subjects will be excluded, provide a justification for doing so*

24. WAIVER OR ALTERATION OF THE CONSENT PROCESS N/A

Complete this section if you are seeking an alteration or complete waiver of the consent process.

- *Describe the possible risks of harm to the subjects involved in this study and explain why the study involves no more than minimal risk to the subject:*
- *Explain why the waiver/ alteration will not adversely affect the rights and welfare of subjects*
- *Explain why it is impracticable to conduct this research if informed consent is required*
- *If appropriate, explain how the subjects will be provided with additional pertinent information after participation. If not appropriate to do so, explain why.*

N/A

*Complete this section if you are obtaining informed consent but you are requesting a waiver of the documentation of consent (i.e., verbal consent will be obtained). To proceed with a waiver based on these criteria, each subject must be asked whether they wish to have documentation linking them to this study. **Only complete subsection 1 OR subsection 2.***

SUBSECTION 1

- *Explain how the only record linking the subject to the research would be the consent document.*
- *Explain how the principal risk of this study would be the potential harm resulting from a breach in the confidentiality*
- *Indicate whether or not subjects will be provided with a written statement regarding the research.*

N/A

SUBSECTION 2

- *Describe the possible risks of harm to the subjects involved in this study and explain why the study involves no more than minimal risk.*
- *Confirm that the research only involves procedure for which consent is not normally required outside the research context.*
- *Indicate whether or not subjects will be provided with a written statement regarding the research.*

N/A

25. WAIVER OF HIPAA AUTHORIZATION

N/A

Complete this section if you seek to obtain a full waiver of HIPAA authorization to use and/or disclose protected health information.

- *Describe the risks to privacy involved in this study and explain why the study involves no more than minimal risk to privacy:*
- *Describe your plan to protect identifiers from improper use or disclosure and to destroy them at the earliest time.*
- *Indicate why it is not possible to seek subjects' authorization for use or disclosure of PHI.*
- *Indicate why it is not possible to conduct this research without use or disclosure of the PHI.*
- *Indicate if PHI will be disclosed outside NSLIJ Health System, and if so, to whom. Note: PHI disclosed outside NSLIJ Health System, without HIPAA authorization needs to be tracked. Please see guidance at www.nslj.com/irb for information about tracking disclosures.*

N/A

Complete this section if you seek to obtain a partial waiver of the patient's authorization for screening/recruitment purposes (i.e., the researcher does not have access to patient records as s/he is not part of the covered entity)

Note: Information collected through a partial waiver for recruitment cannot be shared or disclosed to any other person or entity.

- *Describe how data will be collected and used:*
- *Indicate why you need the PHI (e.g. PHI is required to determine eligibility, identifiers are necessary to contact the individual to discuss participation, other)*
- *Indicate why the research cannot practicably be conducted without the partial waiver (e.g. no access to medical records or contact information of the targeted population, no treating clinician to assist in recruitment of the study population, other)*

We will review the medical records to determine subject eligibility. If a subject is determined to not be eligible for the study, no PHI will be stored. No PHI used for this purpose will be shared with any investigators outside of the institution.

26. VULNERABLE POPULATIONS:

Indicate whether you will include any of these vulnerable populations. If indicated, submit the appropriate appendix to the IRB for review:

- Children or viable neonate*
- Cognitively impaired*
- Pregnant Women, Fetuses or neonates of uncertain viability or nonviable*
- Prisoners*
- NSLIJ Employees, residents, fellows, etc*
- poor/uninsured*
- Students*
- Minorities*
- Elderly*
- Healthy Controls*

If any of these populations are included in the study, describe additional safeguards that will be used to protect their rights and welfare.

N/A

27. MULTI-SITE HUMAN RESEARCH (COORDINATING CENTER)

If this is a multi-site study where you are the lead investigator, describe the management of information (e.g. results, new information, unanticipated problems involving risks to subjects or others, or protocol modifications) among sites to protect subjects.

28. REFERENCES/BIBIOGRAPHY

Provide a reasonable list of references directly related to the study. Any diagrams for new medical devices or brief reprints from journals might also prove useful.

- 1) Nezhat C, Nezhat F, Nezhat C (2008) *Nezhat's Operative Gynecologic Laparoscopy and Hysteroscopy* (3rd ed.). Cambridge University Press
- 2) Maheux-Lacroix S, et al. Hysterosalpingosonography for Diagnosing Tubal Occlusion in Subfertile Women: A Systematic Review Protocol. *Systematic Reviews*. 2013;2:50
- 3) Exacoustos C, et al. Hysterosalpingo-Contrast Sonography Compared with Hysterosalpingography and Laparoscopic Dye Pertubation to Evaluate Tubal Patency. *J Am Assoc Gynecol Lasparosc*. 2003;10(3):367-372
- 4) Marci R, et al. Hysterosalpingocontrast sonography (HyCoSY): evaluation of the pain perception, side effects and complications. *BMC Medical Imaging*. 2013;13:28
- 5) Luciano DE, et al. Contrast Ultrasonography for Tubal Patency. *J Minim Invasive Gynecol*. 2014 Nov-Dec;21(6):994-8
- 6) Graziano A, et al. Sonohysterosalpingography: A suitable choice in infertility work up. *J Med Ultrasonics*. 2013; 40:225-229
- 7) Schankath AC, et al. Hysterosalpingography in the workup of female infertility: indications, technique and diagnostic findings. *Insights imaging*. 2012 Oct;3(5):475-83
- 8) Szymusik I, et al. Factors influencing the severity of pain during hysterosalpingography. *Int J Gynaecol Obstet*. 2015;129(2):118-122
- 9) Handelzalts JE, et al. Information seeking and perceptions of anxiety and pain among women undergoing hysterosalpingography. *Eur J Obstet Gynecol Reprod Biol*. 2016 Jul;202:41-4