IRB-HSR PROTOCOL

Investigator Agreement

BY SIGNING THIS DOCUMENT, THE INVESTIGATOR CONFIRMS:

1. I am not currently debarred by the US FDA from involvement in clinical research studies.
2. I am not involved in any regulatory or misconduct litigation or investigation by the FDA.
3. That if this study involves any funding or resources from an outside source, or if you will be sharing data outside of UVA prior to publication that you will contact the Dean's office regarding the need for a contract and letter of indemnification. If it is determined that either a contract or letter of indemnification is needed, subjects cannot be enrolled until these documents are complete.
4. The proposed research project will be conducted by me or under my close supervision. It will be conducted in accordance with the protocol submitted to and approved by the IRB including any modifications, amendments or addendums submitted and approved by the IRB throughout the life of the protocol.
5. That no personnel will be allowed to work on this protocol until they have completed the IRB-HSR On-line training and the IRB-HSR has been notified.
6. That all personnel working on this protocol will follow all IRB-HSR Policies and Procedures as stated on the IRB-HSR Website http://www.virginia.edu/vprgs/irb/ and on the School of Medicine Clinical Trials Office Website: http://knowledgelink.healthsystem.virginia.edu/intranet/hes/cto/sops/sop_index.cfm
7. I will ensure that all those delegated tasks relating to this study, whether explicitly or implicitly, are capable through expertise, training , experience or credentialing to undertake those tasks.
8. I confirm that the implications of the study have been discussed with all Departments that might be affected by it and have obtained their agreement for the study to take place.
9. That no subjects will be recruited or entered under the protocol until the Investigator has received the signed IRB-HSR Approval form stating the protocol is open to enrollment
10. That any materials used to recruit subjects will be approved by the IRB-HSR prior to use.
11. That all subjects will sign a copy of the most current consent form that has a non-expired IRB-HSR approval stamp.
12. That any modifications of the protocol or consent form will not be initiated without prior written approval from the IRB-HSR, except when necessary to eliminate immediate hazards to the subjects.
13. Any significant findings that become known in the course of the research that might affect the willingness of subjects to enroll or to continue to take part, will be promptly reported to the IRB.
14. I will report immediately to the IRB any unanticipated problems involving risk to subjects or to others including adverse reactions to biologics, drugs or medical devices.
15. That any serious deviation from the protocol will be reported promptly to the Board in writing.
16. That any data breach will be reported to the IRB, the UVa Corporate Compliance and Privacy Office , UVa Police as applicable.
17. That the continuation status report for this protocol will be completed and returned within the time limit stated on the form.
18. That the IRB-HSR office will be notified within 30 days of a change in the Principal Investigator or of the closure of this study.

19. That a new PI will be assigned if the current PI will not be at UVA for an extended period of time. If the current PI is leaving UVa permanently, a new PI will be assigned PRIOR to the departure of the current PI.
20. All study team members will have access to the current protocol and other applicable documents such as the IRB-HSR Application, consent forms and Investigator Brochures.
21. Signed consent forms and other research records will be retained in a confidential manner. Records will be kept at least 6 years after completion of the study.
22. No data/specimens may be taken from UVa without a signed Material Transfer Agreement between OSP/SOM Grants and Contracts Office and the new institution. Original study files are considered institutional records and may not be transferred to another institution. I will notify my department administration regarding where the originals will be kept at UVa. The material transfer agreement will delineate what copies of data, health information and/or specimens may be taken outside of UVa. It will also approve which HIPAA identifiers may be taken outside of UVa with the health information or specimens.
23. If any member of study team leaves UVa, they are STRONGLY ENCOURAGED to use Exit Checklist found on IRB-HSR website at http://www.virginia.edu/provost/facultyexit.pdf.

The IRB reserves the right to terminate this study at any time if, in its opinion, (1) the risks of further experimentation are prohibitive, or (2) the above agreement is breached.

Investigators Experience

Dr. Miller has ABMS Certification in Diagnostic Radiology. His clinical practice experience and current role includes Breast Cancer Screening/Mammograms, Low-dose Breast Tomosynthesis (3D Mammography), Automated Breast Ultrasound System (ABUS), including SOM Assistant Professor and clinical director of the CESM program.

Roger Anderson, Ph.D., is a professor of public health sciences and co-leader for cancer control and population health research. He is internationally known for his work in health disparities and has extensive experience in survey development. Dr. Anderson's primary role in this study is survey development.

Signatures

Principal Investigator

_____	_____	_____
Principal Investigator Signature	Principal Investigator Name Printed	Date

The Principal Investigator signature is ONLY required if this is a new protocol, a 5 year update or a modification changing the Principal Investigator.

Department Chair

BY SIGNING THIS DOCUMENT THE DEPARTMENT CHAIR AGREES:

1. To work with the investigator and with the board as needed, to maintain compliance with this agreement.
2. That the Principal Investigator is qualified to perform this study.
3. That the protocol is scientifically relevant and sound.

_____	_____	_____
Department Chair or Designee Signature	Department Chair or Designee Name Printed	Date

The person signing as the Department Chair cannot be the Principal Investigator or a sub-investigator on this protocol.
The Department Chair or Designee signature is ONLY required if this is a new protocol or a modification changing the Principal Investigator.

Brief Summary/Abstract

Contrast-enhanced spectral mammography (CESM) is an FDA approved tool for breast cancer detection. However, adoption into clinical practice has been slow. In this study, we will explore patient issues related to the use of CESM for breast cancer screening. After receiving the first 50 results from another study (IRB-HSR# pending, Submission #11378) survey of women with dense breasts presenting for screening mammography to understand issues related to convenience, risks, and benefits of advanced screening, we will proceed with this (CESM) study. For this study, 210 women with heterogeneous or dense breast tissue reported on a previous mammogram, will be recruited to undergo a screening Contrast-enhanced Spectral Mammography (CESM). The CESM will serve as the subject's annual screening breast exam for clinical care. A survey will be administered before and after the examination that evaluates the patient experience. Women will not be at high risk for breast cancer (<20% lifetime risk). All abnormal findings will be acted upon independently. Results of the general screening population survey will be compared with those of women who choose to undergo the CESM examination in order to evaluate the influence of age, education, and lifetime risk on decision making about advanced screening.

Background

1. Provide the scientific background, rationale and relevance of this project.

Screening mammography reduces breast cancer mortality by 15-40%. However, the limitations of mammography have long been known regarding the ability to detect cancer in women with dense breast tissue. Interval cancers, presenting as a palpable or other clinical finding between screening intervals, are 5 times more likely in women with heterogeneously dense breast tissue and 17 times more likely in women with extremely dense tissue compared with women with predominately fatty breasts (1). This lack of an effective breast cancer screening modality has prompted breast density legislation- now in effect in 19 states. In 2011, Virginia became the 3rd state to have a breast density law enacted. However, more than 25 million women age 40-74 years have either heterogeneous or dense breast tissue on mammography (2). Any decisions regarding supplemental screening may be costly to our society.

The most common ancillary screening test performed after a mammogram is a screening ultrasound (US). Screening US detects about 30% more breast cancers than mammography alone (3-5). However, screening US is associated with a high false positive rate. Whereas women undergoing screening mammography have a 1-2% risk of undergoing biopsy, 5-7% of women undergoing screening US will be recommended to undergo biopsy. The positive predictive value (PPV) of biopsy recommendation for lesions identified at screening US is also quite low (7-9% cancers, versus 25-40% for mammography). The low specificity is the major downside of using US for ancillary screening of women with dense breast tissue. The cost associated with this examination is high- for every 100 exams performed, up to 7 biopsies will be performed, and up to 10 will have another US in 6 months due to an indeterminate lesion.

Contrast-enhanced spectral mammography (CESM) is an emerging modality that incorporates both anatomic (structural) and functional (enhancement) information of the breasts. CESM is an FDA approved imaging study for detection of breast cancer and is frequently used for diagnostic patients in the UVa Breast Care Center.

There are less than 20 of these units in the U.S., and UVa Cancer Center Breast Program has one. In this exam, patients receive IV iodinated contrast, similar to having a CT scan. After 2 minutes, routine mammographic views are obtained. During the exposure, both high (45-49 KVp) and low (26-30 kVp) energy images are obtained (Figure 1). The low energy exposure is below the "k-edge" of iodine and so the appearance is the same as a conventional mammogram. This high energy exposure will "see" the iodine and the breast tissue. This high energy exposure is subtracted from the low energy exposure to generate an "iodine" image (Figure 2). Because the dense tissue is subtracted out, the CESM is not limited by dense tissue.

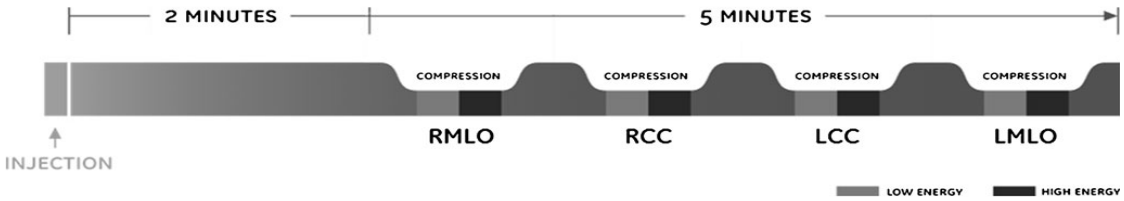
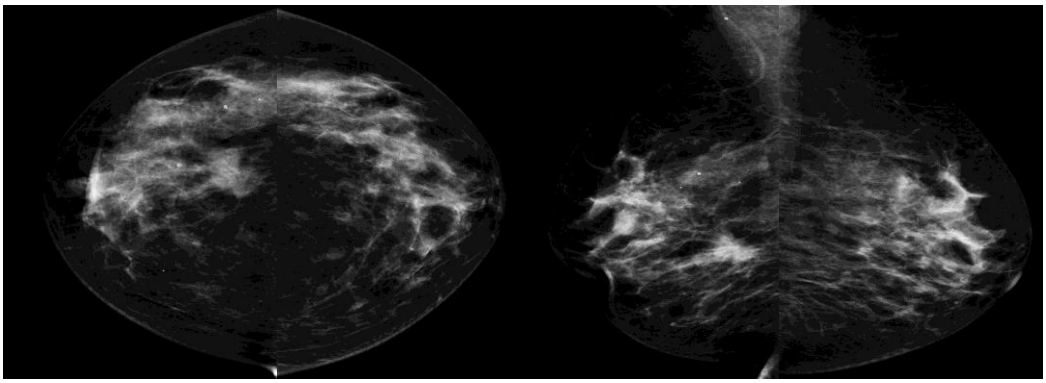


Figure 1. Timing of CESM study



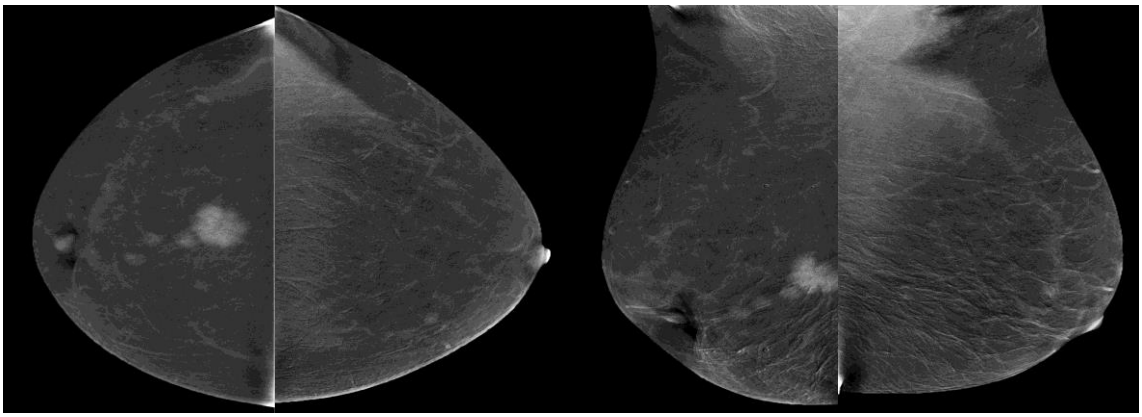


Figure 2. Digital mammogram with dense tissue shows an irregular mass in the posterior right breast (arrows). The CESM study shows this mass as well as three other areas of invasive cancer between the mass and the nipple.

At UVa, about 15 CESM studies are performed per month. The majority are performed for a diagnostic indication such as an abnormal mammogram or MRI, and less are performed for screening. However, screening CESM is often used for women at high risk that cannot undergo breast MRI for various reasons. Nationally, CESM has been slow to be adopted for screening despite the apparent high sensitivity. It is unclear if this is due to lower convenience, concern about IV placement or contrast reaction, or lack of knowledge of this test. The aim of this study is to evaluate patient attitudes related to the use of CESM as a breast cancer screening test.

Hypothesis to be Tested

CESM is an emerging modality that is FDA approved for clinical use. It is possible that this functional test may someday replace breast MRI. While only small studies have been performed to date, one study has demonstrated similar cancer detection, sensitivity, and specificity for CESM compared with breast MRI (6). CESM could be an ideal screening examination for women with dense tissue.

Study Design: Biomedical

1. Will controls be used? No

2. What is the study design?

a) Evaluate the patient experience during a screening CESM to better understand if women find the experience of contrast injection to be too invasive or unpleasant to repeat or recommend to a friend. ("Pre-CESM" and "Post CESM" Surveys)

3. Does the study involve a placebo? No

Human Participants

Ages: 40-69
Sex: **female**
Race: **all**

Subjects- see below

INSTRUCTIONS: For question 1-4 below insert an exact #. Ranges or OPEN is not allowed. This # should be the maximum # you expect to need to enroll (i.e. sign consent) If you are only collecting specimens the number of participants should equate to the # of specimens you need. If you are collecting only data from a chart review the number should designate the number of subjects whose medical records you plan to review. Age/ Sex/Race criteria should designate the demographics of participants from whom you will obtain the specimen/data.

1. **Provide target # of subjects (at all sites) needed to complete protocol.**
   - 210 CESM procedures at the Breast Care Center.

2. **Describe expected rate of screen failure/ dropouts/withdrawals from all sites.**
   CESM rates will be negligible due to pre-screening and study procedure involving only one visit.

3. **How many subjects will be enrolled at all sites?** 210 for CESM at BCC;

4. **How many subjects will sign a consent form under this UVa protocol? 210 for CESM**

5. **Provide an estimated time line for the study.**
   Total 22 months. Enrollment 18 months followed by completion and data analysis

Inclusion/Exclusion Criteria

1. **List the criteria for inclusion** for CESM
   - Female
   - 40 to 69 years
   - Previous normal mammogram (BI-RADS 1 or 2) showing heterogeneous or extremely dense breast tissue within last 24 months
   - Scheduled for screening mammogram as part of the patient's clinical care

2. **List the criteria for exclusion for CESM**
   - No mammogram within last 24 months
   - Fatty or scattered fibroglandular tissue on last mammogram
   - History of allergy to iodinated contrast
   - History of renal disease or renal function abnormalities
   - Pregnant women
   - History of diabetes

- History of paraproteinemia syndromes such as multiple myeloma
- History of collagen vascular disease
- History of vascular disease (coronary artery disease, myocardial infarction, carotid disease, peripheral vascular disease, or known visceral artery disease)
- Previously identified as high risk for breast cancer (>20% lifetime risk)
- Asthma
- Sickle Cell Anemia
- Currently on Dialysis
- If patient is age 60-69 years we will need to confirm that kidney function is normal. We will draw a small volume of blood and check this, unless patient has had a lab test showing normal kidney function in the last 30 days as part of standard of care.

4. List any restrictions on use of other drugs or treatments. none

Statistical Considerations

1. **Is stratification/randomization involved?** No

2. What are the statistical considerations for the protocol?

There are no specific statistical considerations. We are only planning to evaluate women's experience and willingness to undergo CESM in the screening setting. However, it should be noted that if modifications are made to the general survey questionnaire (IRB Submission #11378) after the first 50 patients have completed the questionnaire.

3. Provide a justification for the sample size used in this protocol.

We have funding for 210 screening CESM subjects. This should allow us to evaluate for general attitudes toward CESM as well as some sub-analyses related to factors such as age, and family history. More specifically, we should be able to estimate the percentage of women who have a positive attitude toward CESM within ± 3.5 percentage units. This includes the worst case scenario in which the percentage is 50%, which is the scenario in which a binomial outcome variance is maximized.

4. What is your plan for primary variable analysis?

1. To evaluate the patient experience during a screening CESM to better understand if women find the experience of contrast injection to be too invasive or unpleasant to repeat or recommend to a friend.

Data summarization: Pre and post CESM survey responses that are binary or Likert scaled responses will be summarized by frequencies and percentages. Pre and post CESM survey responses that are continuous scaled responses will be summarized by the mean and standard deviation, the median and interquartile range, and the range of distribution.

Statistical analyses: Pre CESM procedure survey information will be utilized to predict: (a) if patients who undergo CESM are willing to have repeat CESM, and (b) if patients who undergo CESM would recommend CESM to a friend. Multivariate logistic regression will be used to predict these two outcomes. In the former case (a), the outcome variable will indicate if the patient was willing to have a repeat CESM, and in the latter case (b), the outcome variable will indicate if the patient would recommend CESM to a friend. The multivariate logistic regression model predictor variables will include age, level of education, and breast cancer related risk factor variables. Type III Wald tests will be conducted to determine which predictor variables are uniquely associated with outcome. A $p \leq 0.05$ null hypothesis rejection rule will be used as the bases for identifying s unique partial associations.

5. What is your plan for secondary variable analysis?

1. We will evaluate differences by age, education, and risk factors as to whether these drive willingness to undergo CESM.

Data summarization: Binary risk factors will be summarized by frequencies and percentages. Continuous scaled risk factors will be summarized by the mean and standard deviation, the median and interquartile range, and the range of distribution.

Statistical analyses: Multivariate logistic regression will be utilized to determine if there is an association between the willingness to undergo CESM and age, level of education, and breast cancer related risk factors. The outcome variable will be binary and the value 1 will be assigned if the patient is willing to undergo CESM and the value 0 will be assigned if the patient is unwilling to undergo CESM. Predictor variables will include age, level or education, and breast cancer related risk factors. Type III Wald tests will be conducted to determine which predictor variables are uniquely associated with outcome. A $p \leq 0.05$ null hypothesis rejection rule will be used as the bases for identifying s unique partial associations.

2. A secondary endpoint will evaluate differences in recall and PPV for biopsy recommendation compared to our practice norms for women with dense breasts during the same time interval.

Data summarization: Recall frequencies and positive predicted values (PPV) will be summarized in the traditional manner by frequencies and precentages for the former, and by percentages for the latter.

Statistical analyses: Recall fequences and PPV for biopsy recommendation will be compared between the two study-groups by way of exact binomal methods.

6. Have you been working with a statistician in designing this protocol?yes

IF YES, what is their name? James Patrie, Senior Biostatistician, Department of Public Health Sciences.

7. Will data from multiple sites be combined during analysis? No

Biomedical Research

1. What will be done in this protocol?

- Women age 40-69 years of age scheduled to undergo a screening mammogram at any one of our screening sites (Northridge, Orange, Zion Crossroads) or the UVa Breast Care Center will have their previous mammgoram screened to see if there is evidence of heterogeneous or dense breast tissue (within 2 years). If so, the study nurse will contact the patient to see if they would like to participate in the CESM study. All patients having a CESM will have an appointment scheduled at the Breast Care Center, where CESM will be performed.

- In addition, study flyers approved by the IRB will be placed at UVa Imaging sites as well as primary care and gynecology offices.

- All women will have a urine pregnancy test at the Breast Care Center unless there has been no menstual cycle for at least one year (postmenopausal) or history of hysterectomy.

- CESM is a mammogram performed after the injection of contrast via IV. Two images are taken almost simultaneously during the exam after the contrast is administered. The first image is essentially a standard mammogram. The 2nd image shows areas that take up the contrast (enhance) signifying increased blood flow. CESM studies are performed at the UVa Breast Care Center in the West Complex. Contrast administration is given following the same protocol of IV iodinated contrast administration as for CT scans elsewhere in the UVa Health System. Radiologists and technologists in the UVa Breast Care Center are trained in contrast administration and treatment of contrast reaction. Women having a CESM will have a 30 minute period post procedure to monitor for allergy to iodine contrast as per department SOP.

- Per department protocol, women age 60-69 will have serum creatine/GFR within 30 days or will have the test done prior to the CESM exam. If blood needs to be drawn prior to exam a BCC nurse or research nurse will draw 1 green top tube and send this to the Radiology Nursing area in main hospital. The blood will be precessed for Creatinine and GFR on the I-STAT machine, results will be reported back to BCC.The standard mammogram portion of the CESM will be billed to the patients insurance as per standard of care. The administration of contrast and any cost related to the contrast enhanced portion of the CESM, will be paid for by the research study.

- All patients will undergo written consent for study participation after discussion of potential risks and benefits.

- Subjects who agree to participate in the CESM part of the study will complete a short survey regarding their interest and concerns about CESM PRIOR to the examination (Pre CESM Survey).

- The patient will then undergo CESM study which will serve as her annual breast imaging screening in place of annual screening mammogram.

- Since this is a screening exam, the study will not be interpreted immediately by the radiologist.

- Following the exam, the patient will be given a short survey (Post CESM Survey) that evaluates her experience during the CESM examination.

2. List the procedures, in bullet form, that will be done for RESEARCH PURPOSES as stipulated in this protocol.

- Contrast-enhanced Spectral Mammography (CESM) at Breast Care Center
- CESM pre and post surveys for women having CESM procedure only
- Urine pregnancy test for all pre-menopausal women having a CESM at the BCC.

3. Will you be using data/specimens in this study that were collected previously, with the use of a research consent form, from another research study? No

4. Will any of the procedures listed in item # 2 have the potential to identify an incidental finding? This includes ALL procedures, assessments and evaluations that are being done for RESEARCH PURPOSES that may or may not be considered investigational.
Yes. Although the anticipated enhancing lesions are expected to have a high incidence of carcinoma, benign lesions may enhance as well that would not be otherwise detected.

_X__ The examination(s) utilize(s) the same techniques, equipment, etc., that would be used if the subject were to have the examination(s) performed for clinical care. **There exists the potential for the discovery of clinically significant incidental findings.**

- The PI takes full responsibility for the identification of incidental findings:
- The PI will inform the subjects verbally of all incidental findings that are of clinical significance or are of questionable significance**.**
- A follow-up letter describing the finding should be provided to the subject with instructions to either show the letter to their PC or if the subject has no PCP, the subject should be instructed to make an appointment at UVa or at the Free Clinic**.**

5. Do any of the procedures listed above, under question # 2, utilize any imaging procedures for RESEARCH PURPOSES? Yes

IF YES, list procedures: CESM

_x_ This imaging research examination utilizes the same imaging techniques, equipment, scanning sequences that would be used if the subject were to have the imaging performed for clinical care. There exists the potential for the discovery of clinically significant incidental findings.

►If checked, answer the following:

Will the images be read by a licensed radiologist and the reading placed in the subject's medical record? Yes

6. Will you be using viable embryos? No

7. **Will you be using embryonic stem cells?** No

8. Are any aspects of the study kept secret from the participants? No

9. **Is any deception used in the study?** No

10. **If this protocol involves study treatment, explain how a subject will be transitioned from study treatment when they have completed their participation in the study.** N/A

11. Will your study involve measures (C-SSRS/BID/SCID etc.) used to assess for depression and/or suicidality <u>for research purposes? No</u>

Data and Safety Monitoring Plan

INSTRUCTIONS:
If you have any questions completing this section call 243-9847 for assistance.
A Sponsor is defined as entity that will receive data prior to publication.

1. Definition:

1.1 How will you define <u>adverse events</u> (AE)) for this study?

_x__An adverse event will be considered any undesirable sign, symptom or medical or psychological condition **even if the event is not considered to be related** to the investigational drug/device/intervention. Medical condition/diseases present before starting the investigational drug/intervention will be considered adverse events only if they worsen after starting study treatment/intervention. An adverse event is also any undesirable and unintended effect of research occurring in human subjects as a result of the collection of identifiable private information under the research. Adverse events also include any problems associated with the use of an investigational device that adversely affects the rights, safety or welfare of subject s.

1.2 How will you define <u>serious adverse events</u>?

_x__A serious adverse event will be considered any undesirable sign, symptom, or medical condition which is fatal, is life-threatening, requires or prolongs inpatient hospitalization, results in persistent or significant disability/incapacity, constitutes a congenital anomaly or birth defect, is medically significant and which the investigator regards as serious based on appropriate medical judgment. An important medical event is any AE that may not result in death, be life-threatening, or require hospitalization but may be considered an SAE when, based upon appropriate medical judgment, it may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in the definitions of SAEs.

1.3 What is the definition of an unanticipated problem?

Do not change this answer

An unanticipated problem is any event, experience that meets ALL 3 criteria below:

- Is unexpected in terms of nature, severity or frequency given the research procedures that are described in the protocol-related documents AND in the characteristics of the subject population being studies
- Related or possibly related to participation in research. This means that there is a reasonable possibility that the incident may have been caused by the procedures involved in the research study.
- The incident suggests that the research placed the subject or others at greater risk of harm than was previously known or recognized OR results in actual harm to the subject or others

1.4 What are the definitions of a protocol violation and/or noncompliance?

Do not change this answer

A **protocol violation** is defined as any change, deviation, or departure from the study design or procedures of research project that is NOT approved by the IRB-HSR prior to its initiation or implementation. Protocol violations may be major or minor violations.

Noncompliance can be a protocol violation OR deviation from standard operating procedures, Good Clinical Practices (GCPs), federal, state or local regulation**s**. Noncompliance may be serious or continuing.

Additional Information: see the IRB-HSR website at http://www.virginia.edu/vpr/irb/HSR_docs/Forms/Protocol_Violations_%20Enrollment_Exceptions_Instructions.doc

1.5 If pregnancy occurs how will this information be managed?

x_ Other: Pregnancy status is determined prior to mammogram. Pregnancy excludes the subject from the study

1.6 What is the definition of a Protocol Enrollment Exception?

__x__NA- No outside sponsor

1.7 What is the definition of a data breach?

Do not change this answer

A data breach is defined in the HITECH Act (43 USC 17932) as an unauthorized acquisition, access, or use of protected health information (PHI) that compromises the security or privacy of such information.

Additional Information may be found on the IRB-HSR Website: Data Breach

2. Identified risks and plans to minimize risk

2.1 What risks are expected due to the intervention in this protocol?

Expected Risks related to study participation.	**Frequency**
Radiation	____Occurs frequently ____Occurs infrequently _x__Occurs rarely ____Frequency unknown
Allergy to contrast : Mild reactions include: • nausea and vomiting • headache • itching • flushing • mild skin rash or hives Moderate reactions include: • severe skin rash or hives • wheezing • abnormal heart rhythms • high or low blood pressure • shortness of breath or difficulty breathing Severe reactions include: • difficulty breathing • cardiac arrest • swelling of the throat or other parts of the body • convulsions • death profound low blood pressure	____Occurs frequently ____Occurs infrequently __X__Occurs rarely ____Frequency unknown
IV site infection	____Occurs frequently ____Occurs infrequently __X__Occurs rarely ____Frequency unknown

2.2 List by bullet format a summary of safety tests/procedures/observations to be performed that will minimize risks to participants: Adequate screening

2.3 Under what criteria would an INDIVIDUAL SUBJECT'S study treatment or study participation be stopped or modified

__x_At subject, PI or sponsor's request

2.4 Under what criteria would THE ENTIRE STUDY need to be stopped.

INSTRUCTIONS;

- These are called stopping rules for early termination of the entire study.
- List criteria regardless of whether the study is sponsored or not.
- Be sure to include any criteria for which the UVa PI would halt the study at UVa.
- Check all that apply.

_x__Per IRB, PI, DSMB

2.5 What are the criteria for breaking the blind/mask?

__x__NA – Not blinded/masked

2.6 **How will subject withdrawals/dropouts be reported to the IRB prior to study completion?**

__x__IRB-HSR continuation status form

3. Adverse Event / Unanticipated Problem Recording and Reporting

3.1 Will all adverse events, as defined in section 1.1, be collected/recorded? NO

►IF NO, what criteria will be used?

_x__Only adverse events that are deemed related AND serious

3.2 How will adverse event data be collected/recorded?

__x__Spreadsheet: paper or electronic

3.3. How will AEs be classified/graded?

_x__Mild/Moderate/Severe

_X_ Serious/Not serious Required for all protocols

3.4 What scale will the PI use when evaluating the relatedness of adverse events to the study participation?

_x_The PI will determine the relationship of adverse events to the study using the following scale:

Related:	AE is clearly related to the intervention
Possibly related:	AE may be related to the intervention
Unrelated:	AE is clearly not related to intervention

3.5 When will recording/reporting of adverse events/unanticipated problems begin?

___X__After subject begins study intervention

3.6 When will the recording/reporting of adverse events/unanticipated problems end?

_x__ End of study participation

3.7 How will Adverse Events, Unanticipated Problems, Protocol Violations and Data Breaches be reported? Complete the table below to answer this question

Type of Event	To whom will it be reported:	Time Frame for Reporting	How reported?
Any internal event resulting in death that is deemed DEFINITELY related to (caused by) study participation *An internal event is one that occurs in a subject enrolled in a UVa protocol*	IRB-HSR	Within 24 hours	IRB Online and phone call www.irb.virginia.edu/
Internal, Serious, RELATED, Unexpected adverse event	IRB-HSR	Within 7 calendar days from the time the study team received knowledge of the event. *Timeline includes submission of signed hardcopy of AE form.*	IRB Online www.irb.virginia.edu/
Unanticipated Problems that are not adverse events or protocol violations This would include a Data Breach.	IRB-HSR	Within 7 calendar days from the time the study team received knowledge of the event.	Unanticipated Problem report form. *http://www.virginia.edu/vprgs/irb/HSR_docs/Forms/Reporting_Requirements-Unanticipated_Problems.doc)*
Protocol Violations/Noncompliance *The IRB-HSR only requires that MAJOR violation be reported, unless otherwise required by your sponsor, if applicable.* **OR** **Enrollment Exceptions** *See definition- only allowed if*	IRB-HSR	Within 7 calendar days from the time the study team received knowledge of the event.	Protocol Violation, Noncompliance and Enrollment Exception Reporting Form *http://www.virginia.edu/vprgs/irb/hsr_forms.html* *Go to 3rd bullet from the bottom.*

there is a commercial sponsor or a DSMB that has granted the enrollment exception.			
Data Breach	The UVa Corporate Compliance and Privacy Office ITC: if breach involves electronic data Police if breach includes items that are stolen: Stolen on UVA Grounds OR Stolen off UVa Grounds- contact police department of jurisdiction of last known location of PHI	As soon as possible and no later than 24 hours from the time the incident is identified. As soon as possible and no later than 24 hours from the time the incident is identified. IMMEDIATELY.	UVa Corporate Compliance and Privacy Office- Phone 924-9741 **ITC:** Information Security Incident Reporting procedure, http://www.itc.virginia.edu/security/reporting.html UVa Police-Phone- (434) 924-7166

4. **How will the endpoint data be collected/recorded.** Check all that apply

__x__Source documents

5. Data and Safety Oversight Responsibility

5.1. Who is responsible for overseeing safety data for this study?

_x__No additional oversight body other than PI at UVa Skip question 5.2

5.2. What is the composition of the reviewing body and how is it affiliated with the sponsor? n/a

5.3. What items will be included in the aggregate review conducted by the PI?

__x_All adverse events

_____Unanticipated Problems

_____Protocol violations/Issues of noncompliance

_____Audit results

_____Application of dose finding escalation/de-escalation rules

These should be outlined under 2.4.

_____Application of study designed stopping/decision rules

_____Early withdrawals

_____Whether the study accrual pattern warrants continuation/action

_____Endpoint data

5.4 **How often will aggregate review occur?**

For additional information on aggregate review see:
www.virginia.edu/vpr/irb/hsr/continuations.html#aggreview

_x___Annually

5.5. How often will a report, regarding the outcome of the review by the DSMB/DSMC, be sent to the UVa PI? n/a

5.6. How will a report of the information discussed in question 5.4 OR 5.5 be submitted to the IRB?

_x__Part of IRB-HSR continuation status form

Risk/ Benefit Analysis

1. What are the potential benefits for the participant as well as benefits which may accrue to society in general, as a result of this study?

CESM may be an ideal tool for screening women with dense breast tissue compared with screening US, which is currently associated with low specificity and high downstream costs due to unnecessary biopsies. However, there is low utilization of CESM in the screening role. This study will help identify women's attitudes towards CESM as a screening tool.

2. Do the anticipated benefits justify asking subjects to undertake the risks?

Yes. CESM is an FDA approved breast imaging study with extremely low risks. This test could potentially be used broadly in society for screening women with dense breasts, but we need to better understand the barriers to doing so.

Bibliography

1. Boyd NF, Guo H, Martin LJ, et al. Mammographic Density and the Risk and Detection of Breast Cancer. N Engl J Med 2007;356(3):227-236.

2. Sprague BL, Gangnon RE, Burt V, et al. Prevalence of mammographically dense breasts in the United States. J Natl Cancer Inst 2014;106(10):10.1093/jnci/dju255. Print 2014 Oct.

3. Weigert JM, Bertrand ML, Lanzkowsky L, Stern LH, Kieper DA. Results of a Multicenter Patient Registry to Determine the Clinical Impact of Breast-Specific Gamma Imaging, a Molecular Breast Imaging Technique. Am J Roentgenol 2012;198(1):W69-W75.

4. Hooley RJ, Greenberg KL, Stackhouse RM, Geisel JL, Butler RS, Philpotts LE. Screening US in Patients with Mammographically Dense Breasts: Initial Experience with Connecticut Public Act 09-41. Radiology 2012

5. Berg WA, Blume JD, Cormack JB, et al. Combined Screening With Ultrasound and Mammography vs Mammography Alone in Women at Elevated Risk of Breast Cancer. JAMA 2008;299(18):2151-2163.

6. Fallenberg EM, Dromain C, Diekmann F, et al. Contrast-enhanced spectral mammography: Does mammography provide additional clinical benefits or can some radiation exposure be avoided? Breast Cancer Res Treat 2014;146(2):371-381.

APPENDIX: Legal/Regulatory

Recruitment

The following procedures will be followed:

- Finders fees will not be paid to an individual as they are not allowed by UVa Policy.
- All recruitment materials will be approved by the IRB-HSR prior to use. They will be submitted to the IRB after the IRB-HSR has assigned an IRB-HSR # to the protocol.
- Only those individuals listed as personnel on this protocol will recruit and or conduct the consenting process with potential subjects.

Retention Incentives

Any item used by the sponsor/ study team to provide incentive to a subject to remain in the study, other than compensation identified in the Payment section, will be submitted to the IRB for review prior to use. The IRB-HSR will provide the study team with a Receipt Acknowledgement for their records. Retention incentive items are such things as water bottles, small tote bags, birthday cards etc. Cash and gift cards are not allowed as retention incentives.

Clinical Privileges

The following procedures will be followed:

- Investigators who are members of the clinical staff at the University of Virginia Medical Center must have the appropriate credentials and been granted clinical privileges to perform specific clinical procedures whether those procedures are experimental or standard.
- The IRB cannot grant clinical privileges.
- Performing procedures which are outside the scope of the clinical privileges that have been granted may result in denial of insurance coverage should claims of negligence or malpractice arise.
- Personnel on this protocol will have the appropriate credentials and clinical privileges in place before performing any procedures required by this protocol.

- Contact the Clinical Staff Office- 924-9055 or 924-8778 for further information.

Sharing of Data/Specimens

Data and specimens collected under an IRB approved protocol are the property of the University of Virginia. You must have "permission" to share data/ specimens outside of UVa other than for a grant application and or publication. This "permission" may come in the form of a contract with the sponsor or a material transfer agreement (MTA) with others. A contract/ MTA is needed to share the data outside of UVa even if the data includes no HIPAA identifiers and no code that could link the data back to a HIPAA identifier.

- No data will be shared outside of UVa, beyond using data for a grant application and or publication, without a signed contract/MTA approved by the SOM Grants and Contracts office/ OSP or written confirmation that one is not needed.
- No specimens will be shared outside of UVa without a signed contract/MTA approved by the SOM Grants and Contracts office/ OSP or written confirmation that one is not needed.

Prisoners

If the original protocol/ IRB application stated that no prisoners would be enrolled in this study and subsequently a subject becomes a prisoner, the study team must notify the IRB immediately. The study team and IRB will need to determine if the subject will remain in the study. If the subject will remain in the study, the protocol will have to be re-reviewed with the input of a prisoner advocate. The prisoner advocate will also have to be involved in the review of future continuations, modifications or any other reporting such as protocol violations or adverse events.

Prisoner- Individuals are prisoners if they are in any kind of penal institution, such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted. Prisoners may be convicted felons, or may be untried persons who are detained pending judicial action, for example, arraignment or trial.
For additional information see the OHRP website at http://www.hhs.gov/ohrp/policy/populations/index.html

Compensation in Case of Injury

If a subject requests compensation for an injury, the study team should notify the IRB-HSR (924-9634/2439847) the UVa Health System Patient Relations Department (924-8315). As a proactive courtesy, the study team may also notify UVa Health System Patient Safety and Risk Management (924-5595).

On request, the study team should provide the Risk Management Office with the following information/documents:

- Subject Name and Medical Record Number
- Research medical records
- Research consent form
- Adverse event report to IRB
- Any letter from IRB to OHRP

Subject Complaints

During a research study, the study team may receive complaints from a subject. If the study team is uncertain how to respond to a complaint, or is unable to resolve it with the subject, the study team may contact the IRB-HSR (924-9634/243-9847), the UVa Health System Patient Relations Department (924-8315).

Request for Research Records from Search Warrant or Subpoena

If the study team receives a request for research records from a search warrant or subpoena, they should notify UVa Health Information Services at 924-5136. It is important to notify them if information from the study is protected by a Certificate of Confidentiality.

APPENDIX: Recruitment

Recruitment includes identifying, review of records to determine eligibility or any contact to determine a potential subjects interest in the study.

*The UVa HIPAA covered entity is composed of the UVa VP Office of Research, the Health System, School of Medicine, School of Nursing, Nutrition Services (Morrisons), the Sheila C. Johnson Center, the Exercise and Sports Injury Laboratory and the Exercise Physiology Laboratory.

1. How do you plan to identify potential subjects?

- To "identify" a potential subject refers to steps you plan to take to determine which individuals would qualify to participate in your study. This does NOT include steps to actually contact those individuals.
- If your study involves more than one group of subjects (e.g. controls and cases or subjects and caregivers) note below which groups are being identified by the given method.
- Check the methods you plan to utilize:

a._x_ Chart Review/ Clinic Schedule Review/ Database Review from a database established for health care operations (departmental clinical database) or an Improvement Project (*e.g. Performance Improvement, Practice Improvement, Quality Improvement*).
If you plan to obtain data from the UVa Enterprise Data Warehouse (EDW) please see option b below.

DHHS: Study team requests Waiver of Consent to identify potential subjects.

HIPAA: Allowed under Preparatory to Research if PHI to be accessed.

IMPORTANT
Keep in mind that PHI in the medical record may only be accessed by individuals who work under the UVa HIPAA covered entity; which means they meet one of the following criteria:
--a UVa student working in the UVa HIPAA Covered Entity*

--a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

b____ Review of a database that was established to keep data to be used for future research such as the CDR, departmental research database or use of data from a separate current active research protocol.
If you plan to obtain data from the UVa Enterprise Data Warehouse (EDW) you are required to submit your request to the CDR. The CDR staff will work with the EDW to obtain the data you need.

DHHS: Study team requests Waiver of Consent to identify potential subjects.

HIPAA: Allowed under Preparatory to Research if PHI to be accessed.

IMPORTANT
Keep in mind that PHI in the medical record may only be accessed by individuals who work under the UVa HIPAA covered entity; which means they who meet one of the following criteria:
--a UVa student working in the UVa HIPAA Covered Entity*
--a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

The information from which you are obtaining potential subjects must also have an IRB protocol approval. If this item is checked, enter the IRB # below.

IRB# _____

If obtaining information from the Clinical Data Repository (CDR) insert IRB # 10797

c. ____ Patients UVa health care provider supplies the UVa study team with the patients contact information without patients' knowledge.

DHHS: Study team requests Waiver of Consent to identify potential subjects.

HIPAA: Allowed under Preparatory to Research if PHI will be shared by the health care provider.

IMPORTANT
Keep in mind that PHI may only be given to individuals who work under the UVa HIPAA covered entity; which means they meet one of the following criteria:
--a UVa student working in the UVa HIPAA Covered Entity*
--a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

d. _x_ Patient obtains information about the study from their health care provider. The patient contacts the study team if interested in participating. (Health care provider may or may not also be the a member of the study team)

DHHS: NA
HIPAA: Allowed under Health Care Operations

If this choice is checked, check 3d-INDIRECT CONTACT below.

e. __ Potential subjects will not be directly identified. They will respond to an advertisement such as a flyer, brochure etc.

If this choice is checked, check 3d- INDIRECT CONTACT below.
DHHS & HIPAA: NA

f. _____ Potential subjects have previously signed a consent to have their name in a registry/database to be contacted for future studies of this type.

IRB# of registry/ database: _____

DHHS & HIPAA: NA

If item # a, b or c is checked above and if this protocol involves the use of protected health information do you confirm the following to be true? yes

- The use or disclosure is sought solely to review protected health information as necessary to prepare the research protocol or other similar preparatory purposes.
- No PHI will be removed from the UVa covered entity.
- The PHI that the researcher seeks to use or access is necessary for the research purposes.

2. How will potential subjects be contacted?

To "contact" a potential subjects refers to the initial contact you plan to take to reach a potential subject to determine if they would be interested in participating in your study. This may include direct contact by such methods as by letter, phone, email or in-person or indirect contact such as the use of flyers, radio ads etc.

If your study involves more than one group of subjects (e.g. controls and cases or subjects and caregivers) note below which groups are being contacted by the given method.

Check the methods below you plan to utilize:

aXDirect contact of potential subjects by the study team via letter, phone, direct e-mail. Members of study team ARE NOT health care providers of patients. Information will not be collected from psychotherapy notes.

Note: Letter, phone, direct email scripts must be approved by IRB prior to use. See IRB-HSR Website for templates.

DHHS/HIPAA: Study team requests a Waiver of Consent and Waiver of HIPAA Authorization to contact potential subjects.

IMPORTANT:

Keep in mind that if PHI was collected during the identification phase that contact with potential subjects may only be performed by individuals who work under the UVa HIPAA covered entity; which means they meet one of the following criteria:

- a UVa student working in the UVa HIPAA Covered Entity*
- a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

b.____Potential subjects will be approached while at UVa Hospital or Health Clinic by a person who is NOT a member of their health care team. Information will not be collected from psychotherapy notes.

DHHS & HIPAA: Study team requests a Waiver of Consent and a Waiver of HIPAA Authorization to contact potential subjects.

IMPORTANT:
Keep in mind that contacting individuals in a clinical setting may only be performed by individuals who work under the UVa HIPAA covered entity; which means they meet one of the following criteria:
a UVa student working in the UVa HIPAA Covered Entity*
a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

You should share the following information with the potential subject:

- Your name
- Who you are: physician, nurse etc. at the University of Virginia.
- Why you want to speak with them
- Ask if you have their permission to explain the study to them
- If asked about how you obtained their information use one of the following as an option for response.
    - DO NOT USE THIS RESPONSE UNLESS YOU HAVE OBTAINED PERMISSION FROM THEIR UVa PHYSICIAN: Your doctor, Dr. insert name wanted you to be aware of this research study and gave us permission to contact you.
    - We obtained your information from your medical records at UVa.
    - Federal regulations allow the UVa Health System to release your information to researchers at UVa, so that we may contact you regarding studies you may be interested in participating. We want to assure you that we will keep your information confidential.
- IF THE PERSON SEEMS ANGRY, HESITANT OR UPSET, THANK THEM FOR THEIR TIME AND DO NOT ENROLL THEM IN THE STUDY. YOU MAY ALSO REFER THEM TO THE IRB-HSR AT 924-9634.

c. _X_ Direct contact of potential subjects by the study team by approaching in person at UVa or via letter, phone, direct e-mail. Members of study team contacting potential subjects ARE health care providers of patients.

If you are not approaching them in person but using a letter, phone call or direct email please note that the letter, phone, direct email scripts must be approved by IRB prior to use.
See IRB-HSR Website for templates.

DHHS: Study team requests a Waiver of Consent to contact potential subjects
HIPAA: Allowed under Health Care Operations.

d. _x_ Indirect contact (flyer, brochure, TV, broadcast emails, patient provided info about the study from their health care provider and either the patient contacts study team or gives their healthcare provider permission for the study team to contact them.)

The indirect method used (flyer, brochure, TV, broadcast emails) must be approved by the IRB prior to use. The IRB does not need to review any type of script to use when the potential subject responds to the indirect method.

DHHS & HIPAA: NA

e. ____ Potential subjects are not patients. The study does not include obtaining subjects health information. Subjects will be contacted directly via email, phone, letter or presentation in group setting with consent then obtained individually in a private setting.

If you are not approaching them in person but using a letter, phone call or direct email please note that the letter, phone, direct email scripts must be approved by IRB prior to use.
See IRB-HSR Website for templates.

DHHS: Study team requests a Waiver of Consent to contact potential subjects.
HIPPA: NA

3. **Will any additional information be obtained from a potential subject during "prescreening"?** Possibly pre-screening of potential subjects over the telephone or in person to determine their initial eligibility and/or interest in this study.

IF YES, submit any documents that will be used to collect pre-screening information so that the IRB may confirm what questions will be asked.
NOTE: To comply with HIPAA regulations only the minimum necessary information may be collected at this time. This means that only questions pertaining to the Inclusion and Exclusion Criteria may be asked.

IF YES,
DHHS: study team requests a Waiver of Documentation of Consent for Pre-screening questions.

HIPPA:
HIPAA does not apply if:
--no PHI is collected or
--if PHI is collected from a potential subject by an individual from a department that is not part of the HIPAA covered entity.

HIPAA does apply if the collection occurs by individuals* who work in a department that is part of the HIPAA covered entity.

In this case the collection will be covered under Health Care Operations/

These individuals are those that meet one of the following criteria:
--a UVa student working in the UVa HIPAA Covered Entity*
--a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

IF YES, Will any of the questions involve health information?yes

IF YES, will you collect HIPAA identifiers with the health information? yes

IF YES, which HIPAA identifiers will be recorded?MRN, name, age, email

Do you confirm that health information with HIPAA identifiers will not be shared outside of UVa until a consent form is signed or only shared in a de-identified manner? yes

4. **Do you plan to ask the subjects to do anything, other than answering questions, for the study prior to signing a consent?** No

5. **How will the consenting process take place with either the prospective subject, the subject's legally authorized representative or parent/legal guardian of a minor (if applicable)?**

HIPPA:
If the individual, obtaining consent, works under the HIPAA Covered Entity consenting is covered under Health Care Operations.

If the individual obtaining consent does not work under the HIPAA covered entity, HIPAA does not apply.

The potential subject will be interviewed in a quiet and private place and may have family or friends with them if they choose. If there is concern that the potential subject may not be able to read the potential subject will be asked to read the first sentence of the consent form to

determine if they are capable of reading. Depending on the response they will either be offered the opportunity to read the consent form or have the consent form read to them. Once the consent has been read the person obtaining consent will summarize the consent form verbally, asking open ended questions to determine if the potential subject understands what is being covered in the consent form
Potential subjects will be given an opportunity to ask questions. Their level of understanding will dictate how much time will be spent covering each item. Once all of their questions have been answered, if they decide to participate, they will be asked to sign the consent form. The person obtaining consent will sign the form and subjects will be given a copy of the signed consent form. Study procedures will then begin. The informed consent process for each individual subject will be documented in the subject's medical record.

6. Will subjects sign a consent form for any part of the study? yes

7. Will the study procedures be started the same day the subject is recruited for the study? Possibly, as an appointment will be made for the CESM and patient will sign consent before procedure and on day of procedure or they may go through the consent process prior to day of CESM procedure.

8. Is there the potential to recruit economically or educationally disadvantaged subjects, or other vulnerable subjects such as students or employees? yes

IF YES, what protections are in place to protect the rights and welfare of these subjects so that any possible coercion or undue influence is eliminated?
There are students, employees, and economically and educationally disadvantaged people among the patient population at the UVA Health System. We will ask questions to ensure all participants, especially those who are more vulnerable, understand their participation is completely voluntary

9. Do you need to perform a "dry run" of any procedure outlined in this protocol? No

Privacy Plan

The following procedures must be followed.

- The data will be secured per the Data Security Plan of this protocol.
- Only investigators for this study and clinicians caring for the patient will have access to data. They will each use a unique login ID and password that will keep confidential. The password should meet or exceed the standards described on the Information Technology Services (ITS) webpage about *The Importance of Choosing Strong Passwords.*
- Each investigator will sign the University's Electronic Access Agreement forward the signed agreement to the appropriate department as instructed on the form.

If you currently have access to clinical data it is likely that you have already signed this form. You are not required to sign it again.

- UVa University Data Protection Standards will be followed http://www.virginia.edu/informationsecurity/dataprotection.
- If identifiable data is transferred to any other location such as a desktop, laptop, memory stick, CD etc. the researcher must follow the University's "Electronic Storage of Highly Sensitive Data Policy". Additional requirements may be found in the University's Requirements for Securing Electronic Devices.
- If identifiable data is taken away from the UVa Health System, Medical Center Policy # 0218 will be followed.
- Data will be securely removed from the server/drive, additional computer(s), and electronic media according to the University's Electronic Data Removal Policy.
- Data will be encrypted or removed if the electronic device is sent outside of UVa for repair according to the University's Electronic Data Removal Policy.
- If PHI will be faxed, researchers will follow the Health System Policy # 0194.
- If PHI will be emailed, researchers will follow the Health System Policy # 0193 and University Data Protection Standards .
- Data may not be analyzed for any other study without additional IRB approval.
- If you are using patient information you must follow Health System Policy # 0021.
- Both data on paper and stored electronically will follow the University's Record Management policy and the Commonwealth statute regarding the Destruction of Public Records.

Summary of Requirements to Comply with UVa Health System, Medical Center and University Policies and Guidance as noted above:

Highly Sensitive Data is:
-personal information that can lead to identity theft if exposed or
-data that reveals an individual's health condition and/or history of health services use.
Protected Data (PHI) a type of Highly Sensitive Data, is data combined with a HIPAA identifier
Identifiable Data under HIPAA regulations is considered to be *Highly Sensitive Data at UVa.*
A **Limited Data Set** (LDS) under HIPAA regulations is considered to be *Moderately Sensitive Data* at UVa. The only HIPAA identifiers associated with data: dates and or postal address information limited to town or city, state, and zip code.
Will not include subjects age if older than 89 or subjects DOB if older than 89.

Highly Sensitive Data (Identifiable Health Info per HIPAA)	**Moderately Sensitive Data (Limited Data Set and De-identified data per HIPAA)**
General Issues	*General Issues*
Discussions in private Do not share with those not on the study team or those who do not have a need to know.	Do not share with those not on the study team or those who do not have a need to know
Password protect	Password protect
Physically secure (lock) hard copies at all times if not directly supervised. If not supervised hard copies must have double protection (e.g. lock on room OR cabinet AND in building requiring swipe card for entrance).	Physically secure (lock) hard copies at all times if not directly supervised.
For electronic documents turn off File Sharing; turn on firewalls; use up to date antivirus and antispyware; delete data securely.	For electronic documents turn off File Sharing; turn on firewalls; use up to date antivirus and antispyware; delete data securely.
Encrypt See Encryption Solutions Guidance *Files on Health System Network drives are automatically encrypted. If not stored there it is study teams responsibility to make sure data are encrypted.*	
If device sent out for service or repair, encrypt or remove data AND contract for repair using a UVa Purchase order.	If device sent out for service or repair, encrypt or remove data AND contract for repair using a UVa Purchase order.
Store files on a network drive specifically designated for storing this type of data, e.g. high-level security server/drives managed by Information Technology Services or the “F” and “O” managed by Heath Systems Computing Services. You may access it via a shortcut icon on your desktop, but you are not allowed to take it off line to a local drive such as the desktop of your computer (e.g. C drive) or to an individual Use Device*. May access via VPN	
Do not share with sponsor or other outside group before consent is obtained or the IRB has granted appropriate approvals and contract/ MTA is in place	Do not share with sponsor or other outside group before consent is obtained or the IRB has granted appropriate approvals and contract/ MTA is in place
If collected without consent/ HIPAA authorization will NOT be allowed to leave UVa HIPAA covered entity unless disclosure is approved by the IRB and the disclosure is tracked in EPIC	If collected without consent/ HIPAA authorization will NOT be allowed to leave UVa HIPAA covered entity unless disclosure is approved by the IRB and an MTA is in place prior to sharing of data

Highly Sensitive Data (Identifiable Health Info per HIPAA)	**Moderately Sensitive Data (Limited Data Set and De-identified data per HIPAA)**
Electronic Data Collection & Sharing	*Electronic Data Collection & Sharing*
(e.g. smart phone app, electronic consent using tablet etc.) MUST consult with ISPRO or Health System Web Development Office: 434-243-6702 ▪ University Side: IT-Security@virginia.edu ▪ Health System: Web Development Center:	
Individual-Use Device	*Individual-Use Device*
Do not save to individual-use device* without written approval of your Department AND VP or Dean. If approval obtained, data must be password protected and encrypted.	
Do not save an email attachment containing HSD to an individual use device (e.g. smart phone)	
E Mail	*E Mail*
Do not share via email with Outlook Web/ or forward email using other email vendors like Gmail/ Yahoo	
Do not send via email on smart phone unless phone is set up by Health System	
Email may include name, medical record number or Social Security number only if sending email to or from a person with * HS in their email address. *NOTE: VPR & IRB staff do not meet this criteria!*	In addition to sharing LDS, may include initials if persons sending and receiving email work within the UVa HIPAA covered entity.**
FAX	*FAX*
Verify FAX number before faxing	Verify FAX number before faxing
Use Fax Cover Sheet with Confidentiality Statement	Use Fax Cover Sheet with Confidentiality Statement
Verify receiving fax machine is in a restricted access area	Verify receiving fax machine is in a restricted access area
Verify intended recipient is clearly indicated	Verify intended recipient is clearly indicated
Recipient is alerted to the pending transmission and is available to pick it up immediately	Recipient is alerted to the pending transmission and is available to pick it up immediately

Highly Sensitive Data (Identifiable Health Info per HIPAA)	**Moderately Sensitive Data (Limited Data Set and De-identified data per HIPAA)**
Electronic Data Collection & Sharing	*Electronic Data Collection & Sharing*
(e.g. smart phone app, electronic consent using tablet etc.) MUST consult with ISPRO or Health System Web Development Office: 434-243-6702 ▪ University Side: IT-Security@virginia.edu ▪ Health System: Web Development Center:	
Individual-Use Device	*Individual-Use Device*
Do not save to individual-use device* without written approval of your Department AND VP or Dean. If approval obtained, data must be password protected and encrypted.	
Do not save an email attachment containing HSD to an individual use device (e.g. smart phone)	
E Mail	*E Mail*
Do not share via email with Outlook Web/ or forward email using other email vendors like Gmail/ Yahoo	
Do not send via email on smart phone unless phone is set up by Health System	
Email may include name, medical record number or Social Security number only if sending email to or from a person with * HS in their email address. *NOTE: VPR & IRB staff do not meet this criteria!*	In addition to sharing LDS, may include initials if persons sending and receiving email work within the UVa HIPAA covered entity.**
FAX	*FAX*
Verify FAX number before faxing	Verify FAX number before faxing
Use Fax Cover Sheet with Confidentiality Statement	Use Fax Cover Sheet with Confidentiality Statement
Verify receiving fax machine is in a restricted access area	Verify receiving fax machine is in a restricted access area
Verify intended recipient is clearly indicated	Verify intended recipient is clearly indicated
Recipient is alerted to the pending	Recipient is alerted to the pending transmission and

Highly Sensitive Data (Identifiable Health Info per HIPAA)	**Moderately Sensitive Data (Limited Data Set and De-identified data per HIPAA)**
Electronic Data Collection & Sharing	*Electronic Data Collection & Sharing*
(e.g. smart phone app, electronic consent using tablet etc.) MUST consult with ISPRO or Health System Web Development Office: 434-243-6702 University Side: IT-Security@virginia.edu Health System: Web Development Center: Contract must include required security measures.	
May NOT be stored in places like UVaBox, UVaCollab, QuestionPro. May also NOT be stored in non-UVa licensed cloud providers, such as Dropbox, Google Drive, SkyDrive, Survey Monkey, etc.	May be stored in places like UVaBox, UVaCollab, QuestionPro. May NOT be stored in non-UVa licensed cloud providers, such as Dropbox, Google Drive, SkyDrive, Survey Monkey, etc.
LOST OR STOLEN:	*LOST OR STOLEN:*
Must report in accordance with protocol/ in accordance with the Information Security Incident Reporting Policy. Any data breach will also be reported to the IRB of Record if the report meets the criteria of an Unanticipated Problem.	Must report in accordance with protocol/ in accordance with the Information Security Incident Reporting Policy. Any data breach will also be reported to the IRB of Record if the report meets the criteria of an Unanticipated Problem.

** Individual Use Device – examples include smart phone, CD, flash (thumb) drive, laptop, C drive of your computer,*

***The UVa HIPAA covered entity is composed of the UVa VP Office of Research, the Health System, School of Medicine, School of Nursing, Nutrition Services (Morrison's), the Sheila C. Johnson Center, the Exercise and Sports Injury Laboratory and the Exercise Physiology Laboratory.*