
Protocol Title: Shear wave sonoelastography for the noninvasive evaluation of hepatic fibrosis in the pediatric population

Protocol Status: APPROVED

Date Submitted: 11/13/2018

Approval Period: 12/19/2018-01/05/2020

Important Note: This Print View may not reflect all comments and contingencies for approval. Please check the comments section of the online protocol. Questions that appear to not have been answered may not have been required for this submission. Please see the system application for more details.

* * * Continuing Review * * *

Continuing Review Request

WHAT TO UPLOAD WITH YOUR CONTINUING REVIEW APPLICATION

For studies where research activities are limited to data analysis, upload subject safety information and publications (e.g., manuscripts, abstracts) since the last IRB approval, if applicable.

NOTE: if activities are limited to data analysis of de-identified/anonymous data (data that can no longer be linked to subject identifiers directly or through use of a code with master list kept), the study can likely be closed via the Final Report Form. See the SLU IRB Guidance for Closure of Human Subjects Research Studies.

For all other studies, upload:

- Subject safety information including the most current Serious Adverse Event (SAE) cumulative table and data safety monitoring reports since the last IRB approval, if applicable.
- Any publications (e.g., manuscripts, abstracts) since the last IRB approval.

Any changes, updated and/or new study materials should be uploaded and questions 19 - 24 of this form should be completed.

1. **Please indicate the status of the study:**

a) **The study has not started but will become active.**
Please explain why the study has not started.

b) X **The study is ACTIVE (please check the appropriate box below):**
Study is open to accrual.
Study is on hold or halted.
Please explain what needs to occur before accrual can resume.

X **Study is permanently closed to accrual.**

i. Y Have all subjects completed all research related activities/interventions?

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ii. N/A Will the research only remain active for long-term follow-up of subjects?

iii. Y Are remaining research activities limited to data analysis only? (See instructions above).

iv. N For studies that are closed to subject accrual, do any subjects need to be re-consented (to inform them about changes to study procedures, study risks, study personnel, etc.)?

For IRB office use: * may qualify for expedited review

c) **The study has expired and needs to be re-initiated.**
Explain any research activities occurring during lapse in IRB approval.

2.	**Date the study was initially approved by the IRB:**	01/06/2015
3.	**Approval date of previous continuing review:**	12/05/2017
4.	**Total number of participants/records/specimens you are approved to enroll.**	200
5.	**Total number of subjects that have given consent (verbal or written) to date.**	181
6.	**Total number of subjects that failed screening (if not applicable, state N/A).**	9
7.	**Total number of participants accrued since the beginning of the project.**	172
8.	**For multi-center studies, number of subjects approved for accrual study-wide (SLU site plus all other sites).**	NA
9.	**For multi-center studies, number of subjects enrolled study-wide (SLU site plus other sites).**	NA

10. **Number of withdrawals from the research and explanation/reasons for withdrawals.**

None

11. **Description and number of:**

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a) **Reportable Protocol Deviations/Violations since the last approval date:**

NA

b) **Unanticipated Problems (UPs) since the last approval date:**

NA

c) **Serious Adverse Events (SAEs) since the last approval date:Note: Information here should be consistent with the cumulative table, which should also be attached in section #16.**

NA

12. **Have there been any complaints about the research during the last year?** N

If yes, please describe.

13. **Briefly describe the progress of the study to date. Provide a status of participants in study, for example, where is the most recently accrued participant in terms of timeline in the study? If participants are in long-term follow-up, explain what this consists of in terms of data collection and/or intervention. Provide any new information in regard to risks. Summarize or attach publications or presentations.**

There are 78 participants and 88 exams in the liver disease group. Within this group, 11 exams are unusable due to using the linear probe; 5 exams are unusable because they were screen fails. A total of 10 patients had two exams – of which 5 exams were repeated since they were initially done with the linear probe and they returned for another curved exam; another 5 were repeated because they had a second biopsy performed. A total of 72 exams in the liver group have usable data.

There are 93 control patients and 95 control exams. Within the control group, 12 exams were unable to be used due to using the linear probe; 2 are unusable since they were screen fails. A total of 2 patients had a repeat exam since they came back after initially having an exam with a linear probe. A total of 79 exams in the control group have usable data.

Screen fails include those from patients who moved too much, who were too obese to obtain an image, or in whom the liver biopsy was not performed.

14. **Is there a Data Safety Monitoring (DSM) plan for this study?**

Y **No**

Yes, a copy of the DSM report(s) for the last approval period is attached.

Yes, but a copy of the DSM reports(s) for the last approval period is not attached. Please explain below.

15. **FDA Regulated Studies**

Is this a Food and Drug Administration (FDA) Regulated Study, (i.e., involves drugs, devices, biologics)? If yes, please answer the following questions: N

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a) Have there been any changes in the FDA status of any drug or device used in the study?

If yes, please explain:

b) Have any of the investigational drugs or devices used in this study received FDA approval?

If yes, please explain:

c) Have any new alternative drugs or devices been approved for treatment of the study condition that may affect subjects willingness to participate?

If yes, please explain:

Have current subjects been notified? Please explain:

d) Has there been a change in the standard care that may be considered as an alternative to the investigational drug or device or that would affect the original study design?

If yes, please explain:

Have current subjects been notified? Please explain:

e) Is there any new information that might affect the risk/benefit ratio and the willingness of current study subjects to participate or to continue to participate in the research?

If yes, please explain:

Have current subjects been notified? Please explain:

f) Does the study include an investigator's brochure (IB)?

If yes, what is the current version date?

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(If study has multiple IBs, attach current versions in Attachments section (#16))

16. **Provide a summary of any recent findings, literature, or other relevant information (especially pertaining to risks), if applicable.**

NA

17. **Have there been any significant amendments or revisions to the protocol during the past approval period? (Significant amendments include changes in study design or risk level including those that resulted in a change in consent).** N

If yes, please briefly summarize the changes:

18. Y The consent materials attached to this eIRB application (including consent documents, assent documents, recruitment statements or other materials used to obtain consent) are the versions being used in the conduct of this study and all enrolled subjects have signed consent forms on file, if required. (If the requirement to obtain consent was waived or if no participants have enrolled since last continuing review, check N/A).

NOTE: The IRB routinely monitors consent document usage and may request copies of redacted participant consent forms.

19. **Are any changes (amendments) requested with this Continuing Review?**

Yes, please complete the remainder of this form.

Y **No, form is complete. Please submit.**

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

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

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

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

If no, please justify why not.

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

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

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24. Are consent documents modified?

Proceed to the appropriate section(s) of the protocol and make your changes. Also make necessary changes in the Consent Form(s), Assent Form(s), Recruitment Statement, Questionnaire, or other attachments, as applicable. Upload any revised IRB materials. Please provide the entire revised document (not just revised pages). Use track changes or highlight (in yellow) changes to documents being revised. Please upload a tracked/highlighted copy of each revised document to be stamped upon IRB approval. NOTE: Upload a clean copy (changes or highlights removed) of documents in file formats other than Microsoft Word (i.e., the IRB will remove the tracked changes/highlights on uploaded Word documents).

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

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

Expedited Paragraphs

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* * * Personnel Information * * *

Study Personnel Roles:
-Principal Investigator: accepts responsibility for study, must sign obligations, can edit protocol and submit to IRB
-Administrative Contact: additional study contact, may or may not also be member of research team, can edit/prepare protocol and submit to IRB
-Key Personnel (Research Team): SLU member of research team, can view protocol (not edit)
-Non-SLU Collaborator: member of research team from another institution or organization outside of SLU, has no access to system, must be provided with PDF of protocol. NOTE: SLUH/SSM employees who collaborate regularly may obtain a guest SLU account if access to system is needed.
-Department Chair: Official Department Chair, may or may not also be a member of research team, can view the protocol (not edit). NOTE: a proxy may be listed if the Chair is the PI.

IMPORTANT NOTE: Human Subjects Protection Training is mandatory for all research team personnel.

Principal Investigator (PI) Mandatory

PI must be SLU affiliate.

Name of Principal Investigator (Faculty, Staff or Student)	Degree (MD/PhD)	Title
Farmakis, Shannon	MD	Assistant Professor
Email	**Phone**	**Fax**
farmakis@slu.edu	314-577-5649	
Department Name		
Radiology		

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Human Subjects Training Completed? Y
WARNING: Proof of training must show below or the application will be returned. If your training information isn't showing, upload a copy in the Attachments section.

Research Experience ***?HELP?***

involvement with prior retrospective clinical research studies during residency and fellowship training and with laboratory research while in medical school

Research Team Member Duties Picklist

1.	X	Recruitment	2.	X	Obtains consent
3.	X	Determine Subject Eligibility for Accrual	4a.		Subject Physical Examinations
4b.		Follow-up Visits including physical assessments	5.	X	Perform study procedures or Specimen Collection
6a.		Administer and/or Dispense Study Drugs, Biologics or Devices (must be licensed)	6b.		Receive, Store, Manipulate or Account for Study Drugs, Biologics or Devices
7.		Subject Randomization or Registry	8.	X	Collection of Subject Data
9.	X	Report Data (CRFs, e-CRFs, Spreadsheets)	10.	X	Data Analysis
11a.	X	Review Adverse Events	11b.	X	Treat and Classify Adverse Events
12.		Other (Please insert explanation below.)			

No training data is available.

Administrative Contact

Name of Administrative Contact	Degree	Title
Kitchell, Robin		Administrative Assistant
Hardy, Anna	RN, MPH	Research Nurse

Key Personnel (Research Team)

Name of Key Personnel (Research Team)	Degree	Title	Department Name
Tao, Ting	MD	Assistant Professor	Radiology
Teckman, Jeffrey	MD	Professor	Pediatrics
Jain, Ajay	M.D.	Assistant Professor	Pediatrics
Guzman, Miguel	M.D.	Assistant Professor	Pathology
Caudill, Karen	M.D.	Assistant Professor	Radiology

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Department Chair Mandatory

The official Department Chair should be listed here. If the Department Chair is the PI, a proxy may be listed.

Name of Department Chair	Degree	Title
Brown, Jeffrey	MD	Professor

Email	Phone	Fax
jjbrown@slu.edu	(314) 268-5780	

Department Name
Radiology

Is this individual also a member of the research team? N

Human Subjects Training Completed?
WARNING: Proof of training must show below or the application will be returned. If your training information isn't showing, upload a copy in the Attachments section.

Research Experience *?HELP?*

Research Team Member Duties Picklist

1.	Recruitment	2.	Obtains consent
3.	Determine Subject Eligibility for Accrual	4a.	Subject Physical Examinations
4b.	Follow-up Visits including physical assessments	5.	Perform study procedures or Specimen Collection
6a.	Administer and/or Dispense Study Drugs, Biologics or Devices (must be licensed)	6b.	Receive, Store, Manipulate or Account for Study Drugs, Biologics or Devices
7.	Subject Randomization or Registry	8.	Collection of Subject Data
9.	Report Data (CRFs, e-CRFs, Spreadsheets)	10.	Data Analysis
11a.	Review Adverse Events	11b.	Treat and Classify Adverse Events
12.	Other (Please insert explanation below.)		

No training data is available.

Research Team Roles

Name(s), Degree	Department	Experience	Duties
Farmakis, Shannon, MD	Radiology	involvement with prior retrospective clinical research studies during residency and fellowship training and with laboratory research while in medical school	Recruitment, Obtains consent, Determine Subject Eligibility for Accrual, Perform study procedures or Specimen Collection, Collection of Subject Data, Report Data (CRFs, e-CRFs, Spreadsheets), Data Analysis, Review Adverse

			Analysis, Review Adverse Events, Treat and Classify Adverse Events
Hardy, Anna, RN, MPH	Radiology	Anna has been involved with clinical and retrospective research in the past and she will be supervised by Dr. Farmakis.	Recruitment, Obtains consent, Subject Randomization or Registry, Collection of Subject Data, Data Analysis
Tao, Ting, MD	Radiology	8 years of bench research, 4 years experience with retrospective clinical studies while in residency training	Recruitment, Obtains consent, Determine Subject Eligibility for Accrual, Perform study procedures or Specimen Collection, Collection of Subject Data, Report Data (CRFs, e-CRFs, Spreadsheets), Data Analysis
Teckman, Jeffrey, MD	Pediatrics	>20 years experience as both PI and Co-I with multiple clinical trials	Recruitment, Obtains consent, Determine Subject Eligibility for Accrual, Report Data (CRFs, e-CRFs, Spreadsheets), Data Analysis, Review Adverse Events, Treat and Classify Adverse Events
Jain, Ajay, M.D.	Pediatrics	PI and Co-I in multiple clinical trials	Recruitment, Obtains consent, Determine Subject Eligibility for Accrual, Perform study procedures or Specimen Collection, Collection of Subject Data, Report Data (CRFs, e-CRFs, Spreadsheets), Data Analysis, Review Adverse Events, Treat and Classify Adverse Events
Guzman, Miguel, M.D.	Pathology	Currently involved in a clinical trial with Harbor-UCLA Medical Center (NIH grant support). Prior research experience in clinical translation research in anatomic pathology, pediatric pathology and neuropathology. Bench research experience with different techniques in anatomic pathology including histochemistry, immunohistochemistry and electron microscopy.	Other (Please insert explanation below.) histopathologic evaluation of subject specimen

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Caudill, Karen, M.D.	Radiology	involvement with research during training	Recruitment, Obtains consent, Determine Subject Eligibility for Accrual, Perform study procedures or Specimen Collection, Collection of Subject Data, Report Data (CRFs, e-CRFs, Spreadsheets), Data Analysis

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* * * Subject Population * * *

Subject Population(s) Checklist

Select All That Apply :

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

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* * * Study Location * * *

Study Location(s) Checklist

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

- [X] Saint Louis University, Medical Center Campus
- [ ] Saint Louis University, Frost Campus
- [ ] Saint Louis University, Madrid Campus
- [ ] Saint Louis University, SLUCare Practice Locations
- [ ] SSM STL (DePaul Hospital, St. Mary's Health Center, St. Joseph (St. Charles, Wentzville, Lake Saint Louis), St. Clare)
- [X] Cardinal Glennon Children's Medical Center
- [ ] Saint Louis University Hospital (SSM Health- SLU Hospital)
- [ ] SLU-SSM Cancer Center Research Alliance Sites

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Other (In the box below, list any off-campus institutions or locations and describe the activities being conducted there. Please provide letters of cooperation and/or IRB approvals from each location to document support/approval of the study. You may provide such documentation as it becomes available, but you may not begin work at those sites until documentation of support is provided to the IRB.) Please refer to the Guidance for involving non-SLU institutions in human subject research.

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* * * General Checklist * * *

General Checklist

Select All That Apply :

- [ ] Collection of Specimens
- [ ] Data collection via e-mail or the Internet
- [ ] Deception/Incomplete Disclosure
- [ ] Dietary Supplements, Vitamins, and Other Food Agents
- [X] FDA Approved Device
- [ ] FDA approved drugs, reagents, other chemicals administered to subjects (even if they are not being studied), or biologic products
- [ ] Genetic Testing
- [ ] HIV Testing
- [ ] Human blood, cells, tissues, or body fluids
- [ ] International Research or Research on International Populations
- [ ] Investigational drugs, reagents, chemicals, or biologic products
- [ ] Investigational Device
- [ ] Investigator Initiated Study *?HELP?*
- [X] Medical Records
- [ ] Photography, Video, or Voice-Recording Subjects
- [ ] Questionnaires and/or tests
- [ ] Radioisotopes/radiation-producing machines, even if standard of care
- [ ] rDNA/Gene Transfer Therapy
- [ ] Registry(ies)
- [ ] Specimens to be stored for future research projects (must be in consent form)
- [X] Study of existing data or specimens
- [X] University Indemnified Study (SLU is responsible for liability coverage) *?HELP?*
- [ ] Other (clarify in text box to the right)

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

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* * * Funding * * *

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Funding Checklist

NONE

Funding - Saint Louis University

What type of Saint Louis University funding?	SLU eRS #
Grant submitted to President's Research Fund	8878
Liver Center grant--Grant submitted	N/A

Funding - Industry Sponsor

Sponsor Name	Sponsor's Protocol Version Date
GE Healthcare Ltd.	

Funding - Other

Name of Other Funding source	SLU eRS #
Cardinal Glennon Foundation--Grant application in process	N/A

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

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* * * Expedited Paragraphs * * *

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

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

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

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

b) Research on medical devices for which

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Title

Shear wave sonoelastography for the noninvasive evaluation of hepatic fibrosis in the pediatric population

Complete Sections 1 - 16. In sections that allow reference to sponsor protocol or grant, clearly state section and page numbers. Any information that is different or specific to the local site should be in the SLU application. Specify N/A as appropriate.

1. Background

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

a) **Provide an introduction and background information. Describe past experimental and/or clinical findings leading to the formulation of the study, if applicable. Investigator Initiated studies must cite references in the response provided or attach a bibliography. *?HELP?***

The evaluation of pediatric liver disease continues to be a major focus of research both in well-characterized liver diseases and in liver fibrosis secondary to obesity. The degree of fibrosis is generally well-accepted as both a measurement of disease severity and a prognostic indicator. Unfortunately, the current gold standard to assess fibrosis remains a liver biopsy, which, in addition to anesthesia risks and sampling errors, can result in profound hemorrhage, infections, and even mortality. Standard and reliable noninvasive biomarkers of hepatic fibrosis in the pediatric population are greatly needed. Sonoelastography has emerged as a method of evaluating liver disease. Three methods of quantitative sonoelastography are currently in use.

Transient elastography is an M-mode based sonographic technique in which a mechanical vibrator creates a low-frequency wave causing shear stress in the tissue at a fixed depth in the target tissue. It has gained widespread use in evaluation of liver fibrosis in the adult population (Fibroscan); however, its use has great limitations in the pediatric population as it does not use real-time ultrasonography (B mode) and has a fixed depth in which the measurement is taken. The lack of real-time imaging makes it impossible to accurately select an area for appropriate sampling, and the fixed depth is not appropriate for very young children with smaller livers. Also, the shock wave that is administered has not been tailored for use in young children. Furthermore, this technique is very unreliable in patients that are obese or who have ascites.

Other methods of sonoelastography include Acoustic Radiation Force Impulse Imaging (ARFI) and Shear Wave Elastography (SWE). The latter is also known as supersonic shear wave imaging. Both of these techniques use real-time ultrasonography and administer focused high-intensity, short-duration (acoustic radiation) pulses to produce shear waves in the target tissue. Neither technique is limited by the presence of ascites as the shear waves propagate through the fluid. ARFI uses a single pushing beam to generate the shear waves, and the propagation of those shear waves are monitored using conventional pulse-echo ultrasound at various off-axis lateral locations. The speed of the shear wave in the tissue is determined by collecting the displacement through time. This principle of elastography is based on the Young modulus using the formula: $E=3\rho V2$ (E elasticity's modulus, V speed, ρ density of the tissue). The degree of tissue displacement is then used to create an elastogram. Limitations of ARFI include a small selected region of interest (ROI) (10 mm x 5 mm), it is a 1-dimensional technique, and it is unable to provide a corresponding elasticity map of the tissue. The latter also prevents retrospective evaluations of the tissue elasticity.

SWE is the newest elastography technique. It works by generating a localized radiation force that travels faster down the acoustic axis than the shear wave speed producing tiny, almost simultaneous, displacements in the tissues at all positions along the acoustic axis. The generated shear wave is shaped like a cone or fan, known as the Mach cone. An ultrafast

sonography is then performed which provides a side-by-side greyscale image and color-coded elasticity map of the tissue in the ROI. The ROI is displayed in real time B-mode imaging and, thus, represents a 2-dimensional technique. Advantages include a larger, fan-shaped ROI (up to 50mm x 50mm), and the acquisition of a quantitative map of liver tissue stiffness with corresponding greyscale ultrasound image. As a result, simultaneous viewing of the selected region of interest provides better anatomic detail with a corresponding color map of the tissue elasticity which may result in more accurate scoring of the stage of fibrosis. The presence of a color map also allows for retrospective analysis.

Only a few studies have begun to use ARFI to analyze liver fibrosis in the pediatric population. Studies using SWE for evaluation of liver fibrosis are also limited and all but one have been performed in adults; however, early studies have shown it to be an accurate method for liver fibrosis staging. Tutar, et al safely performed a study using SWE in pediatric patients in Turkey. No dedicated pediatric studies have been performed in the United States, as the technology was just recently approved for use in adults by the FDA. The use of this device in pediatrics represents an off-label use. That being said, SWE has safety considerations that are similar to Doppler mode which is a standard ultrasound technology performed in pediatric patients of all ages. While it has a higher thermal index than routine B-mode ultrasound, it is measured to be within the safety limits set by the American Institute of Ultrasound in Medicine (AIUM).

b) **Describe any animal experimentation and findings leading to the formulation of the study, if there is no supporting human data.**

N/A

2. Purpose of the study

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

Background: Pediatric liver disease continues to remain a major focus of research. This has taken on greater relevance with the rise in pediatric obesity which, in addition to several other well-characterized liver diseases, causes liver fibrosis. The degree of fibrosis is well-accepted as both a measurement of disease severity and a prognostic indicator. Unfortunately, the current gold standard to assess fibrosis remains a liver biopsy, which, in addition to anesthesia risks and sampling errors, can result in profound hemorrhage, infections, and even mortality. Thus, there is a great need for reliable, non-invasive biomarkers of hepatic fibrosis. Sonoelastography has emerged as a method of evaluating liver disease.

Specific Aims: To perform shear wave elastography (SWE) on pediatric patients with known liver disease who undergo a liver biopsy in order to determine the accuracy of SWE in evaluating the various stages of liver fibrosis using the METAVIR histopathologic scale. We will also perform SWE on patients without liver disease to establish baseline measurements in a normal liver.

Potential Impact: SWE may represent an accurate, reliable, and noninvasive method of staging liver fibrosis in pediatric patients and may obviate the need for performing liver biopsies in evaluating liver disease in these patients.

Protocol Title: Shear wave sonoelastography for the noninvasive evaluation of hepatic fibrosis in the pediatric population

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

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

Hypothesis: We hypothesize that shear wave sonoelastography (SWE) measurements will correlate with the histopathologic assessment of liver fibrosis in pediatric patients.

Specific Aims: To perform SWE on pediatric patients with known liver disease who undergo a liver biopsy within one month of the ultrasound exam in order to determine the accuracy of SWE in evaluating the various stages of liver fibrosis using the METAVIR histopathologic scale. As a control, we will perform SWE on patients without liver disease to establish baseline measurements in a normal liver.

Please save frequently

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

The study design is a prospective single blind control experiment. Subject recruitment will be ongoing as patients who undergo routine liver biopsy in order to evaluate their liver disease will also undergo an ultrasound with sonoelastography. The minimum number of patients required in the test group in order to determine accuracy of the research test is 100. Study recruitment for patients without liver disease will be stopped once 100 patients are enrolled. An additional 8 months will be required for study analysis.

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

N/A

3. Study Procedures

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

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

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

If No, explain what SLU will NOT participate in:

Please save frequently

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

b) **Describe all the procedures, from screening through end-of-study, that the human subject must undergo in the research project, including study visits, drug treatments, randomization and the**

procedures that are part of standard of care. Specify which procedures are for research and which are standard of care. Please note: The box below is for text only. If you would like to add tables, charts, etc., attach those files in the Attachment section (#16).

Any pediatric patient (0-18 years of age) with known liver disease in whom a liver biopsy is to be performed as standard of care to assess the degree of fibrosis will also undergo an abdominal ultrasound to evaluate the liver. The ultrasound is also standard of care. Informed consent will then be obtained from the patient's parent or guardian with verbal assent from the patient for the perfomance of a shear wave sonoelastography exam as part of the research study. The research portion of the ultrasound exam will be performed at the same time as the standard of care ultrasound exam. The ultrasound must be performed within 1 month of the liver biopsy. No additional visits or treatments are required of the patients beyond what they would normally have as part of their routine treatment or medical care following the liver biopsy. Following the liver biopsy and ultrasound exam, the patients involvement in the study is complete. The patient's electronic medical record will be reviewed for pertinent clinical information including history, laboratory values, and liver biopsy results.

Underlying diagnoses include but are not limited to biliary atresia, congenital fibrosis-cholestasis, Alagille syndrome, Caroli's disease, choledochal cyst, alpha-1-antitrypsin deficiency, progressive familial intrahepatic cholestasis (PFIC), viral hepatitis, glycogenosis, fructosemia, Wilson disease, cystic fibrosis, autosomal recessive polycystic kidney disease (ARPCKD), mesenterico-caval shunt, post liver transplant, and nonalcoholic steatohepatitis (NASH).

In addition, any pediatric patient (0-18 years of age) undergoing evaluation with an abdominal ultrasound as standard of care for evaluation for a diagnosis other than liver disease and in whom the US shows a normal liver, gallbladder, pancreas, spleen, and biliary tree will then be asked to enroll in the research study by undergoing shear wave elastography. Following completion of the exam, the patient's involvement in the study will be complete. No additional follow up appointments or study visits are required. Liver biopsies are not to be performed in this group of patients.

The biopsy will be obtained as random sample, preferably from the right lobe of the liver, by the pediatric gastroenterologists as this is the area that the sonoelastography measurements will also be obtained. This should reduce sampling error and result discordance. The liver biopsy must be obtained within 1 month of the ultrasound exam.

Histolopathologic evaluation will be performed using the Ishak and METAVIR classification systems by pathologists blinded to elastography results. These classifications systems are part of the standard of care evaluation of the biopsy material. Only the liver biopsy results in the patient's chart will be reviewed as part of the study.
Ishak:
0: No fibrosis
1: Fibrous expansion of some portal areas, with or without short fibrous septa
2: Fibrous expansion of most portal areas, with or without short fibrous septa
3: Fibrous expansion of most portal areas with occasional portal to portal (P-P) bridging
4: Fibrous expansion of portal areas with marked bridging [portal to portal (P-P) as well as portal to central (P-C)]
5: Marked bridging (P-P and/or P-C) with occasional nodules (incomplete cirrhosis)
6. Cirrhosis, probably or definite
METAVIR:
F0: no portal fibrosis
F1: portal fibrosis without septa
F2: portal fibrosis with few septa
F3: portal fibrosis with numerous septa but non cirrhosis
F4: cirrhosis

Shear wave ultrasound—Using 2 probes (C1-6 which is a low frequency curved probe and L9 which is a high-frequency linear probe) on the the GE Logiq E9, the selected area of interest (ROI) will be in the right lobe of the liver or in a portion of a transplant liver. The ROI will be an area away from vessels and bile ducts using an intercostal or subcostal approach. Ten separate acquisitions will be obtained on each patient by the attending radiologist and sonographer who are blinded to the results of the liver biopsy. The mean value will be used.

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

N/A

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

The results of the SWE using the velocity measurements displayed on the elastography map with a quantitative color map that is expressed in kPa (kiloPascals) will be correlated with the stage of fibrosis using the METAVIR scale from the liver biopsy results in order to determine the accuracy of SWE in evaluating the various degrees of liver fibrosis. The statistical analysis will include Receiver Operating Characteristic curves as well as scatter plots and box plots. The mean and median values as well as a range of the SWE measurements will be correlated with the individual METAVIR stages of fibrosis (F0-F4), and a p value will be calculated for each stage to assess the accuracy of SWE based on individual fibrosis stages. Further statistical analysis will also be performed to compare results of SWE and histopathology in subgroups of liver disease patients, such as those with NASH compared to those without. Scatter plots will be used to compare the SWE results in normal patients to those with liver disease.

Please save frequently

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

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

If yes, please describe the standard of care and standard practice at SLU for the

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condition/disease/situation being studied.

The current standard of care for evaluation of pediatric patients with liver disease includes routine abdominal ultrasounds and liver biopsy in order to determine the stage of fibrosis.

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

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

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

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

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* * * Radioisotopes or Radiation Machines * * *

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

4. Radioisotopes or Radiation Machines

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

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

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

a) **If applicable, list and quantify the radiographic diagnostic and therapeutic procedures associated with this protocol by clicking "Add" and adding to Table 1 below. (Includes X-ray, fluoroscopy, CT, radioactive materials, nuclear medicine, PET-CT, radiation oncology, accelerator, Cyber Knife procedures, etc.)**

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b) Total estimated research radiation dose * :

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

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

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* * * Devices * * *

5. Devices

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

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

FDA Approved Devices

Device Name	Manufacturer	Provide IDE #. Documentation of IDE # required unless imprinted on sponsor protocol (attach in section #16).
Logiq E9 Diagnostic Ultrasound System	GE	Nonsignificant risk. The device has FDA approval for use in adults and now in children as well

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

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

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Phase III Phase IV Not Phased

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

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

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

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

Please read the IND Statements.

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* * * Other Levels Of Review * * *

7. Other Levels Of Review

1. University Radiation Safety

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

X **Not Applicable**

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

2. Institutional Biosafety

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

information.

X **Not Applicable**

Yes, study requires Institutional Biosafety review

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

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

X **Not Applicable**

Yes, study requires PTNT review

4. Saint Louis University Hospital

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

X **Not Applicable**

Yes, study requires Saint Louis University Hospital review

5. SSMSL

All research involving SSMSL locations (including Cardinal Glennon), including inpatient or outpatient services and medical record access, requires approval from the SSM STL or SSM Cardinal Glennon Research Business Review (RBR) prior to study initiation. This process is designed to facilitate compliance with state and federal regulations as they pertain to research in hospitals and clinical research billing. While researchers can begin to complete the SSM RBR form at any time, the form should not be submitted until the IRB and the CTO have approved the study. Please contact the SSMSL Office at 989-2058 or Marcy.Young@ssmhealth.com for more information.

Not Applicable

X **Yes, study requires RBR review**

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

Registration may be required if any of the following apply: 1) The project meets the FDAAA definition of an "Applicable Clinical Trial", which requires registration on ClinicalTrials.gov. 2) As of January 1, 2017, a new NIH policy mandated biomedical and behavioral "Clinical Trials" to be registered on ClinicalTrials.gov. In addition, NIH policies require personnel on NIH "Clinical Trials" to take GCP training every three years. 3) Registering may be required for Journal Publication (ICMJE). Please review relevant definitions here. Contact the CTO at clinical-trials-office@slu.edu with questions about registering on ClinicalTrials.gov and refer to the training page of the IRB website for information on NIH GCP Training requirements.

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* * * Subject Population * * *

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

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

0-18 years

b) Number of evaluable subjects to be accrued at SLU or SLU site (this includes all sites under the direction of the SLU PI). **200**

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

c) Number of evaluable subjects to be accrued study wide. *?HELP?* **200**

d) If including vulnerable populations (minors, pregnant women and fetuses, neonates, non-English speaking, economically or educationally disadvantaged, prisoners, adults temporarily or permanently unable to consent for themselves): 1) provide the rationale for the importance of including this population in the research, and 2) specify the measures being taken to minimize risks to potentially vulnerable subjects. Click on hyperlinks to access SLU Guidelines containing additional considerations and strategies for mitigating risks.

The study is specifically designed to evaluate the effectiveness of shear wave elastography in determining liver fibrosis in pediatric patients. The shear wave elastography exam has no risks as it is a noninvasive and non-radiation based imaging test. There are no risks to the patients. Routine ultrasound exams and liver biopsies being performed in these patients is part of standard of care treatment.

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

If minors are of age of assent but are mentally unable to provide consent, parental consent will be obtained. The minor will be made aware of the study to the best of our ability and the decision will be left up to the parents at that point. Parents will be clearly be made aware that the age of the child would normally require their assent but because of the education level of their child the assent is not obtained.

f) **If any specifically targeted subjects are students, employees, or laboratory personnel, specify the measures being taken to minimize the risks and the chance of harm to these potentially vulnerable subjects. See SLU Guidelines for additional considerations and strategies for mitigating risks.**

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

Potential subjects with known liver disease will be recruited by the pediatric gastroenterologists as these patients would be undergoing ultrasound evaluation and liver biopsy as part of standard of care treatment. These patients would be presented with a recruitment statement form during their clinic visit. During their exam in radiology, explanation of the procedure would be performed by the radiologist who would then obtain consent from the parent and informed assent from the child. Potential control patients will be recruited by giving them a recruitment statement and copy of the consent form as they check-in to the radiology department for an abdominal exam ordered by a physician as part of standard clinical care. The form will inform them that they may be asked to participate in the study following the exam. If deemed eligible by the radiologist, the radiologist will then obtain consent from the parent and informed assent from the child. Recruitment will also occur via flyers posted in the radiology department and GI clinics.

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* * * Subject Population * * *

8. Subject Population (continued)

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

h) **Inclusion and Exclusion Criteria.**

Identify inclusion criteria.

Inclusion criteria:
Test population: Any pediatric patient (0-18 years of age) with known liver disease with plans to undergo a liver biopsy within 1 month of ultrasound exam. Underlying diagnoses include but are not limited to biliary atresia, congenital fibrosis-cholestasis, Alagille syndrome, Caroli's disease, choledochal cyst, alpha-1-antitrypsin deficiency, progressive familial intrahepatic cholestasis (PFIC), viral hepatitis, glycogenosis, fructosemia, Wilson disease, cystic fibrosis, autosomal recessive polycystic kidney disease (ARPCKD), mesenterico-caval shunt, post liver transplant, and nonalcoholic steatohepatitis (NASH). Written informed consent from parent or legal guardian. Informed assent from the child.

Control population: Any pediatric patient (0-18 years of age) undergoing an abdominal ultrasound for reasons other than liver disease and in whom the US shows a normal liver, gallbladder, pancreas, spleen, and biliary tree. Written informed consent from parent or legal guardian. Informed assent from the child. In addition, the patients that have undergone biopsy and have shown no histologic evidence

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of fibrosis will also serve as a control population. The elastography measurements of these patients will be compared to those obtained in the pediatric patients without a history of liver disease in whom the ultrasound exam of the abdomen was found to be normal.

Identify exclusion criteria.

Exclusion criteria: Inconclusive biopsy results. Patient not cooperative for the ultrasound exam. Failure to give informed consent. No biopsy results within allotted time frame. Poor acoustic window in which to perform sonoelastography.

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

No compensation will be provided for participation in the study for the initial study group unless patients were asked to come back in for an additional ultrasound because original data was unusable. In that case, they will receive $50 for their visit if they live within 40 miles and $100 if they live further out to cover the cost of the additional travel and additional time required to Cardinal Glennon for the ultrasound exam visit required for participation.

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

Study related costs will be covered by intramural and possible extramural funding. The patient will not be charged for any costs related to the shear wave elastography exam. Costs of patient office visits, liver biopsy, and routine ultrasound exams will be paid by the patient or insurance company as these are considered standard of care treatment methods.

k) **Estimate the probable duration of the entire study including data analysis and publication. This estimate should include the total time each subject is to be involved and the duration the data about the subject is to be collected. If the study is Investigator-initiated, a timeline for individual subject recruitment, follow-up, total time for subject accrual, and data analysis for the study is required.**

The total recruitment process for control patients is estimated to take one year. The total recruitment process for test subjects is expected to take 18 months. The data analysis is expected to take 3 months.

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* * * Risks * * *

9. Risks

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

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

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

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

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

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

no more than minimal risk

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

loss of confidentiality

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

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

N/A

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

no more than minimal risk

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

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

The shear wave sonoelastography exam will be terminated on a patient if the patient is uncooperative. The loss of confidentiality will be minimized by having the recorded data on an encrypted USB device which is password protected. The physical data will be kept in a locked file cabinet in a locked office to which only the PI has access.

10. **Reproductive Risks.**

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

N/A

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

N/A

11. Data Safety Monitoring

Federal regulations require that when appropriate, the research protocol makes adequate provisions for monitoring the data to ensure the safety of participants. Monitoring should be commensurate with risks and with the size and complexity of the research, and could range from no plan needed to an independent data safety monitoring board. Please refer to SLU Guidelines for Data and Safety Monitoring as you complete the questions below.

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

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

If no, please justify why not.

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

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

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

If no, please justify why not.

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

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

b. Will there be language barriers and if so, how will they be addressed?

Note: If materials are to be distributed to subjects in their native language, please follow SLU's Guidance For Studies Involving Non-English Speaking Subjects.

NOTE: Export control laws include the transfer of technical information and data, as well as information and technology to foreign nationals. If this study has international components, contact the SLU Export Control Officer for direction on whether export control policies apply.

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

10. Benefits/Alternatives

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

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participants.

There is no potential benefit to the subjects. The results of the study may benefit future subjects and/or society in general as if shear wave sonoelastography is found to be an accurate method of evaluating the degree of liver fibrosis in pediatric patients, it may reduce or obviate the need for liver biopsies in patients with liver disease. In addition, if the number of required liver biopsies in these patients is reduced or eliminated, the risks associated with performing sedation in these patients is also reduced or eliminated.

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

Nonparticipation

11. Procedures to Maintain Confidentiality and Privacy

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

Confidentiality

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

For the questions below, please use the following definitions:

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

Coded: data in which (1) identifying information, such as name or social security number, has been replaced with a number, letter, symbol, or combination thereof (i.e., the code), and (2) a key to decipher the code exists enabling linkage of data to identifying information (e.g., a master list), and (3) the key (master list) is kept separately from coded data; AND/OR

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

a) **Electronic (Computer) Data**

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

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

Not Applicable, No Electronic (Computer) Data

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

b) Hardcopy (Paper) Data

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

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

Not Applicable, No Hardcopy (Paper) Data

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

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

USB devices used at SSM Cardinal Glennon Children's Medical Center are encrypted devices which are password protected. Anyone trying to access the information on the drive without the correct password will not be able to see what information the device contains. In addition, the data on the device will be accessed through the username/password secured SSM network. The data obtained from the patient's medical record will be kept on a data collection sheet which will then be kept in a locked cabinet in a locked office. The information that will be obtained from the patient's medical record includes birthdate, current age, gender, height, weight, BMI, history of known liver disease, labs (total bilirubin, AST, ALT, GGTP, cytokeratin-18), liver biopsy results, and reports of abdominal ultrasounds.

d) If data or specimens are being shared outside of the research team, indicate who will receive the material, specifically what they will receive (data or specimens), and if an agreement has been signed to cover the transfer. Note: unless covered under a Clinical Trial or other agreement, the transfer of data or specimens to an external entity will require an agreement. For the transfer of materials (specimens), a Materials Transfer Agreement (MTA) is used; for the transfer of data, a Data Use or Data Transfer Agreement is used. Please contact the Research Innovation Group at 314-925-3027 for assistance.

N/A

e) If samples or data will be provided to SLU from an outside source, indicate whether you will have access to identifiers, and if so, how identifiable information is protected. Note: unless covered under another agreement (e.g., Clinical Trial Agreement or subcontract), the transfer of data or specimens from an external entity to SLU may require an agreement. For the transfer of materials (specimens), a Materials Transfer Agreement (MTA) may be required; for the transfer of data, a Data Use or Data Transfer Agreement may be required. Please contact the Research Innovation Group at 314-925-3027 for

assistance.

N/A

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

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

h) Describe any study-specific (non standard of care) information or documentation that will be put in the participants' medical records for this research (e.g., study visit notes, lab results, etc.). If none, state "not applicable". NOTE: documentation of research in Epic should be done in accordance with the SLUCare Epic Research Charting Policy and Clinical Workflow: Documenting Research Encounters in Epic.

N/A

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

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

Privacy

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

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

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

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

Use of drapes or other privacy measures

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

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

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X Consideration of parental inclusion/absence for studies involving minors

Other (please explain):

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* * * Potential Conflict of Interest * * *

12. Potential Conflict of Interest

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

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

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

Check all those that apply:

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

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

1. A Conflict of Interest Management Plan.

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has been approved for all investigators for this study
is pending
has not been initiated

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

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

Investigator(s) must have:

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

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

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

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* * * Informed Consent * * *

13. Informed Consent

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

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

State N/A if not applicable.

1) **How is consent being obtained? When and where will the discussion take place? If the study involves a Non-English Speaking participant/population, please include details about plans for translated consent materials and interpreters to be used (see SLU Guidelines for Involving Non-English Speaking Subjects for more details).**

Consent will be obtained by any of the four pediatric radiologists on the IRB proposal who will discuss the research study and explain the shear wave elastography exam with the parent/guardian and child while in the ultrasound exam room in the radiology department while they are there for their routine abdominal ultrasound or prior to a scheduled liver biopsy in the endoscopy suite, patient

their routine abdominal ultrasound or prior to a scheduled liver biopsy in the endoscopy suite, patient room, or radiology department.

2) **If the study involves adults unable to consent for themselves (whether diminished capacity to consent is temporary, permanent, progressive or fluctuating), please address the following: a) how is capacity to provide consent being assessed (initially and throughout study, if applicable); b) if unable to provide consent, how is LAR being determined (See SLU LAR Guidelines); c) if unable to provide consent, will assent be obtained and if not, why not?; d) if unable to provide assent, will dissent be honored and if not, why not? Note: participants initially unable to provide consent for themselves are expected to be given an opportunity to provide consent once capacity is gained. See SLU Guidelines for Adults Unable to Provide Consent for additional detail.**

In patients that are old enough for assent but are cognitively impaired to a point of being unable to give assent we would allow the parents or guardians to make the decision about participation. We will make every effort to assent the patient to best of their ability.

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

Informed Consent

Title	Consent Type	Attached Date
Approved_CR2017_Addendum Consent	Consent	12/06/2017
Approved_CR2017_Control Consent FDA app...	Consent	12/06/2017
Approved_CR2017_Test patients Consent F...	Consent	12/06/2017

* * * Assent * * *

14. Assent

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

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

Yes, unless they are developmentally delayed and are unable to give assent, then it will be left up to the parent/guardian for the decision to participate, but we will still go over the assent with the patient and make every effort to inform them to best of our ability.

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

No

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

Research team members involved in consenting are pediatric health care providers with training in childhood development. Comprehension and willingness will be based on the researchers interaction with the adolescent. Parental input will be considered but will not supersede the investigator's analysis of the child's willingness to participate.

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

Assent Documents

Title	Upload assent document	Attached Date
Approved_ CR2017_Assent_CHILDREN_Clinic. ..	Approved_CR2017_Assent_CHILDREN_Clinical normal control	12/06/2017
Approved_CR2017_Assent_CHILDREN_Clinical	Approved_CR2017_Assent_CHILDREN_Clinical_	12/06/2017
Approved_CR2017_Assent_ADOLESCENTS_Clin..	Approved_CR2017_Assent_ADOLESCENTS_Clinical	12/06/2017
Approved_CR2017_Assent_ADOLESCENTS_Clin.	Approved_CR2017_Assent_ADOLESCENTS_Clinical normal control	12/06/2017

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* * * HIPAA * * *

15. HIPAA

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

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

No health information. HIPAA does not apply.

X Yes (continue to question 2).

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

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

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

City/State/Zip codes

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

Age (if subjects are 90+ years)

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

X Names

Social Security numbers

Telephone numbers

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

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

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

Fax numbers

Electronic mail addresses

X Medical record numbers

Health plan beneficiary numbers

Account numbers

Certificate/license numbers

Vehicle identifiers and serial numbers, including license plate numbers

Device identifiers and serial numbers

Web Universal Resource Locations (URLs)

Internet Protocol (IP) address numbers

Biometric identifiers, including finger and voice prints

Full face photographic images and any comparable images

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

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3. **Sources of Protected Health Information:**
   - X Hospital/medical records for in or out patients
   - X Physician/clinic records
   - X Laboratory, pathology and/or radiology results
   - Biological samples
   - X Interviews or questionnaires/health histories
   - Mental health records
   - Data previously collected for research purposes
   - Billing records
   - Other

   Please describe:

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

   X Not applicable (continue to question 5).

   Only linkable code that can link data to the identity of the subject. A code access agreement or business associate agreement may be needed when data are shared with other non-SLU entities. If necessary, the agreement can be added and uploaded in item #5, below.

   Limited identifiers: Zip codes, dates of birth, or other dates only. The study qualifies as a Limited Data Set. A data use agreement may be needed when data are shared with other non-SLU entities. If necessary, the agreement can be added and uploaded in item #5, below, using DUA-external option.

   With unlimited identifiers. The consent document and HIPAA Authorization form must describe how the information will be disclosed.

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

HIPAA Documents

HIPAA Documents	Title	Attached Date
HIPAA Authorization	Approved_Version 2 HIPAA authorization	01/22/2015

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* * * Attachments * * *

16. Attachments

In this section, please upload additional documents associated with your protocol. Failure to attach files

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associated with the protocol may result in the protocol being returned to you.

Possible documents for this protocol could include:

- Bibliography
- Cooperating Institution's IRB Approval
- Data Collection Sheet
- Debriefing Script
- Device Information/Documentation
- Grant Proposal/Sub-Contract
- Human Subjects Training Certificate/Proof of Training
- Information Sheet/Brochure
- Interview/Focus Group Questions
- Investigator's Brochure
- Letter of Agreement/Cooperation
- IND Application Letter
- Package Insert
- Patient Diary Form
- Questionnaire/Survey
- Recruitment Material (e.g., flyers, ads, e-mail text)
- Safety Information (DSM Information)
- Scientific/PPC Review or Department Chair Review
- Sponsor's Protocol
- Sponsor's Protocol Amendment
- Study Design Chart/Table
- Other files associated with the protocol (most standard formats accepted: pdf, jpg, tiff, mp3, wmv, etc.)

To update or revise any attachments, please delete the existing attachment and upload the revised document to replace it.

Document Type	Document Name	Attached Date	Submitted Date
Bibliography	Bibliography IRB	10/30/2014	11/14/2014
Human Subjects Training Certificate/Proof of Training	CITI certificate	10/30/2014	11/14/2014
Device Information/Documentation	K142160 LOGIQ E9 R5 Clearance Letter	11/04/2014	11/14/2014
Letter of Agreement/Cooperation	Logiq E9 brochure	11/05/2014	11/14/2014
Device Information/Documentation	LOGIQ E9 Shear Wave USA Sell Sheet	11/05/2014	11/14/2014

Device Information/Documentation	LOGIQ E9 Timeline-USA	11/05/2014	11/14/2014
Human Subjects Training Certificate/Proof of Training	Tao CITI FCOI	11/07/2014	11/14/2014
Human Subjects Training Certificate/Proof of Training	Tao CITI SLU	11/07/2014	11/14/2014
Human Subjects Training Certificate/Proof of Training	Tao CITI training	11/07/2014	11/14/2014
Device Information/Documentation	Device Nonsignificant Risk Justification	12/16/2014	12/16/2014
Data Collection Sheet	Approved_Data collection sheet	01/22/2015	01/22/2015
Recruitment Material (e.g., flyers, ads, e-mail text)	Approved_SWE model_recruitment_statement for test population	01/22/2015	01/22/2015
Recruitment Material (e.g., flyers, ads, e-mail text)	Approved_SWE normal model_recruitment_statement	01/22/2015	01/22/2015
Committee Approvals	SSM RBR Approval Letter Farmakis SLU #25138	03/05/2015	03/27/2015
Recruitment Material (e.g., flyers, ads, e-mail text)	Approved_Flyer for SWE	04/02/2015	04/02/2015
Other	Highlighted K152195 LOGIQ S8 R3 510k Clearance Letter	12/18/2015	12/18/2015
Other	K152195 LOGIQ S8 R3 510k Clearance Letter	12/18/2015	12/18/2015
Other	Approved_SWE Clarification Letter	01/08/2016	01/08/2016
Publications (e.g., manuscripts, abstracts)	SPR 2017 meeting submission FINAL	12/09/2016	12/09/2016
Publications (e.g., manuscripts, abstracts)	SPR 2017 Figure 1	12/09/2016	12/09/2016
Publications (e.g., manuscripts, abstracts)	SPR 2017 Figure 2	12/09/2016	12/09/2016
Publications (e.g., manuscripts, abstracts)	SPR 2017 Table 1	12/09/2016	12/09/2016
Human Subjects Training Certificate/Proof of Training	A Hardy CITI COI desc	10/06/2017	10/06/2017

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Human Subjects Training Certificate/Proof of Training	A Hardy CITI IRB desc	10/06/2017	10/06/2017

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* * * PI Obligations * * *

PI Obligations

By clicking the box below you indicate that you accept responsibility for and will follow the ethical guidelines set forth by the Belmont Report, Declaration of Helsinki, the Nuremberg Code, and the Ethical Principles of the American Psychological Association (if applicable) for the research described. It also indicates that you have the requisite funding, credentials, training, and any necessary hospital privileges, if needed, to carry out all procedures and treatments involved in the protocol.

Clicking the box also affirms that the activities involving human subjects will not begin without prior review and approval by the Institutional Review Board, and that all activities will be performed in accordance with state and federal regulations and Saint Louis University's assurance with the Department of Health and Human Services. The PI assures that if members of the SLU research team access protected health information (PHI) from a covered entity in order to seek consent/authorization for research or to conduct research, such access is necessary for the research, is solely for that purpose, and the information will not be removed from the covered entity without IRB authorization or approved waiver. PI further assures that the SLU research team will comply with the terms of a Data Use Agreement to PHI (if any).

1) Have you completed the annual Conflict of Interest in Research Disclosure Form? Y

You can only select N/A if you are not currently listed on any externally funded research projects nor listed on any proposals for externally funded research support.

NOTE: An annual disclosure must be completed by all faculty, staff and students involved in the design, conduct or reporting of externally funded research applications and awards.

2) Have your financial interests changed significantly since you completed the annual disclosure form? N

The PRINCIPAL INVESTIGATOR certifies that he/she has read the University's Conflict of Interest Research Policy and has checked the appropriate box in the 'Potential Conflict of Interest' section of the application. In addition, the PRINCIPAL INVESTIGATOR certifies that, to the best of his/her knowledge, no person working on this project at SLU has a conflict of interest or if a conflict of interest does exist, that an appropriate management plan is in place.

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According to the Saint Louis University Conflict of Interest in Research Policy, as PI, it is your responsibility to inform co-investigators, staff, or students involved in the design, conduct, or reporting of externally sponsored research of their requirement to complete a Conflict of Interest in Research Disclosure Form.

X **I accept this responsibility.**

X **The Principal Investigator has read and agrees to the above certifications and will abide by the above obligations.**

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* * * Event History * * *

Event History

Date	Status	View Attachments	Letters
12/19/2018	CONTINUING REVIEW 4 FORM APPROVED	Y	N
12/14/2018	CONTINUING REVIEW 4 FORM REVIEWER(S) ASSIGNED		
12/07/2018	CONTINUING REVIEW 4 FORM PANEL REASSIGNED		
11/24/2018	CONTINUING REVIEW 4 FORM PANEL REASSIGNED		
11/13/2018	CONTINUING REVIEW 4 FORM SUBMITTED	Y	
11/12/2018	CONTINUING REVIEW 4 FORM CREATED		
07/23/2018	AMENDMENT 10 FORM DELETED		
06/22/2018	AMENDMENT 10 FORM CREATED		
12/06/2017	CONTINUING REVIEW 3 FORM APPROVED	Y	N
11/27/2017	CONTINUING REVIEW 3 FORM REVIEWER(S) ASSIGNED		
11/21/2017	CONTINUING REVIEW 3 FORM PANEL MANAGER REVIEW		
11/20/2017	CONTINUING REVIEW 3 FORM PANEL REASSIGNED		

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11/08/2017	CONTINUING REVIEW 3 FORM SUBMITTED	Y	
11/08/2017	CONTINUING REVIEW 3 FORM CREATED		
10/11/2017	AMENDMENT 9 FORM APPROVED	Y	N
10/11/2017	AMENDMENT 9 FORM REVIEWER(S) ASSIGNED		
10/06/2017	AMENDMENT 9 FORM RESUBMITTED	Y	
10/04/2017	AMENDMENT 9 FORM RETURNED		
10/04/2017	AMENDMENT 9 FORM PANEL REASSIGNED		
10/03/2017	AMENDMENT 9 FORM SUBMITTED	Y	
09/18/2017	AMENDMENT 9 FORM CREATED		
03/03/2017	AMENDMENT 8 FORM DELETED		
03/03/2017	AMENDMENT 8 FORM CREATED		
12/21/2016	CONTINUING REVIEW 2 FORM APPROVED	Y	N
12/09/2016	CONTINUING REVIEW 2 FORM REVIEWER(S) ASSIGNED		
12/09/2016	CONTINUING REVIEW 2 FORM PANEL MANAGER REVIEW		
12/09/2016	CONTINUING REVIEW 2 FORM PANEL REASSIGNED		
12/09/2016	CONTINUING REVIEW 2 FORM RESUBMITTED	Y	
12/08/2016	CONTINUING REVIEW 2 FORM RETURNED		
12/08/2016	CONTINUING REVIEW 2 FORM PANEL REASSIGNED		
12/08/2016	CONTINUING REVIEW 2 FORM PANEL MANAGER REVIEW		
12/08/2016	CONTINUING REVIEW 2 FORM PANEL REASSIGNED		
12/08/2016	CONTINUING REVIEW 2 FORM SUBMITTED	Y	

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12/08/2016	CONTINUING REVIEW 2 FORM CREATED		
07/29/2016	AMENDMENT 7 FORM APPROVED	Y	N
07/27/2016	AMENDMENT 7 FORM REVIEWER(S) ASSIGNED		
07/21/2016	AMENDMENT 7 FORM PANEL REASSIGNED		
07/18/2016	AMENDMENT 7 FORM SUBMITTED	Y	
07/18/2016	AMENDMENT 7 FORM CREATED		
06/10/2016	AMENDMENT 6 FORM APPROVED	Y	Y
05/27/2016	AMENDMENT 6 FORM REVIEWER(S) ASSIGNED		
05/26/2016	AMENDMENT 6 FORM PANEL MANAGER REVIEW		
05/19/2016	AMENDMENT 6 FORM PANEL REASSIGNED		
05/11/2016	AMENDMENT 6 FORM SUBMITTED	Y	
05/03/2016	AMENDMENT 6 FORM CREATED		
01/08/2016	AMENDMENT 5 FORM APPROVED	Y	Y
01/07/2016	AMENDMENT 5 FORM REVIEWER(S) ASSIGNED		
12/18/2015	AMENDMENT 5 FORM PANEL REASSIGNED		
12/18/2015	REPORT 1 FORM APPROVED	Y	Y
12/18/2015	AMENDMENT 5 FORM SUBMITTED	Y	
12/18/2015	AMENDMENT 5 FORM CREATED		
12/17/2015	REPORT 1 FORM REVIEWER(S) ASSIGNED		
12/17/2015	REPORT 1 FORM PANEL REASSIGNED		
12/17/2015	REPORT 1 FORM SUBMITTED	Y	

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12/17/2015	REPORT 1 FORM CREATED		
12/16/2015	CONTINUING REVIEW 1 FORM APPROVED	Y	Y
12/04/2015	CONTINUING REVIEW 1 FORM REVIEWER(S) ASSIGNED		
12/03/2015	CONTINUING REVIEW 1 FORM PANEL MANAGER REVIEW		
11/18/2015	CONTINUING REVIEW 1 FORM PANEL REASSIGNED		
11/09/2015	CONTINUING REVIEW 1 FORM SUBMITTED	Y	
11/09/2015	CONTINUING REVIEW 1 FORM CREATED		
08/28/2015	AMENDMENT 4 FORM APPROVED	Y	Y
08/28/2015	AMENDMENT 4 FORM UNDO APPROVED		
08/28/2015	AMENDMENT 4 FORM APPROVED	Y	Y
08/28/2015	AMENDMENT 4 FORM REVIEWER(S) ASSIGNED		
08/27/2015	AMENDMENT 4 FORM RESUBMITTED	Y	
08/27/2015	AMENDMENT 4 FORM RETURNED		
08/19/2015	AMENDMENT 4 FORM SUBMITTED	Y	
08/17/2015	AMENDMENT 4 FORM CREATED		
07/01/2015	AMENDMENT 3 FORM APPROVED	Y	Y
06/30/2015	AMENDMENT 3 FORM REVIEWER(S) ASSIGNED		
06/26/2015	AMENDMENT 3 FORM SUBMITTED	Y	
06/26/2015	AMENDMENT 3 FORM CREATED		
04/02/2015	AMENDMENT 2 FORM APPROVED	Y	Y
04/01/2015	AMENDMENT 2 FORM REVIEWER(S) ASSIGNED		

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03/31/2015	AMENDMENT 2 FORM RESUBMITTED	Y	
03/31/2015	AMENDMENT 2 FORM RETURNED		
03/27/2015	AMENDMENT 2 FORM SUBMITTED	Y	
03/27/2015	AMENDMENT 2 FORM CREATED		
01/28/2015	AMENDMENT 1 FORM APPROVED	Y	Y
01/27/2015	AMENDMENT 1 FORM REVIEWER(S) ASSIGNED		
01/27/2015	AMENDMENT 1 FORM PANEL REASSIGNED		
01/27/2015	AMENDMENT 1 FORM SUBMITTED	Y	
01/27/2015	AMENDMENT 1 FORM CREATED		
01/22/2015	NEW FORM APPROVED	Y	Y
01/21/2015	NEW FORM REVIEWER(S) ASSIGNED		
01/14/2015	NEW FORM SUBMITTED (CYCLE 3)	Y	
01/08/2015	NEW FORM CONTINGENT		
12/19/2014	NEW FORM REVIEWER(S) ASSIGNED		
12/17/2014	NEW FORM PANEL MANAGER REVIEW		
12/17/2014	NEW FORM PANEL REASSIGNED		
12/16/2014	NEW FORM SUBMITTED (CYCLE 2)	Y	
12/15/2014	NEW FORM SUBMITTED (CYCLE 1)	Y	
12/08/2014	NEW FORM CONTINGENT		
11/17/2014	NEW FORM REVIEWER(S) ASSIGNED		
11/14/2014	NEW FORM PANEL ASSIGNED		
11/14/2014	NEW FORM SUBMITTED	Y	

Protocol Title: Shear wave sonoelastography for the noninvasive evaluation of hepatic fibrosis in the pediatric population

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11/14/2014	NEW FORM PREREVIEWED
11/14/2014	NEW FORM PREAPPROVAL
11/14/2014	NEW FORM PREAPPROVAL
10/21/2014	NEW FORM CREATED