Date Initially Completed: 3/24/2016 **or Date Updated:** 5/9/2016			**IRB # (if known):** 4837
Protocol Title:	Shear wave elastography in native kidney disease: a pilot study		
Protocol Version/ Date:	5/9/2016		
Sponsor:	AES grant		
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Please carefully review and complete each section of this form. If your study already has a separate protocol (e.g. developed by a sponsor or submitted as part of a grant application), you have the option to reference the section and page numbers of that protocol where appropriate in this form. PLEASE NOTE: many of the questions below are looking specifically for what will be happening locally to protect participants. This information is generally not found in a protocol written for multiple sites.

NOTE: Depending on the nature of your research, certain sections below may not be applicable. Indicate "N/A" as appropriate. You must provide a response for each section. DO NOT DELETE SECTIONS OR LEAVE SECTIONS BLANK.

Keep an electronic copy of this form. You will need to modify this form when making changes to the protocol.

1) Protocol Abstract (*Briefly (in 250 words or less) describe the study in language understandable to a layperson. Include a brief description of the study purpose, target disease/condition if applicable, key eligibility criteria, and main study interventions*): Kidney biopsy is the primary technique to assess the degree of kidney damage and disease progression. However, this procedure is costly and has complications including bleeding, infection and patient discomfort. It is also impractical to perform biopsies on patients who are ill or have bleeding tendencies. The ultrasound technique has been used for many years to assess kidney structure and status. However, it is not accurate or reliable at quantifying the degree of fibrosis (long term damage) of diseased kidneys. Interestingly, a promising new ultrasound technique called shear wave elastography (SWE) has been developed to assess tissue stiffness. This technique has been studied previously in transplanted kidneys with promising results. It has only been done in few studies on native kidneys and these studies had major limitations. Our study will attempt to build upon these prior studies and overcome their shortcomings by comparing results obtained by SWE across a broad range of patients with kidney disease as assessed by biopsy results. We are aiming to determine whether SWE can serve as a non-invasive marker of kidney fibrosis. This technique can serve as a marker to follow up the rate of progression of kidney disease besides laboratory tests. More importantly, SWE has the potential to revolutionize practice by helping clinicians make decisions about getting a kidney biopsy.

2) Project Objectives and Hypotheses: Objective: To determine whether differences exist in elasticity measurements between native kidneys with and without fibrosis.
Hypothesis: Kidneys with higher grades of fibrosis will demonstrate higher (up to x 1.5) measures of tissue elasticity and stiffness compared to kidneys with zero fibrosis.

3) Background/Significance of Research (*Provide the scientific or scholarly background and rationale for the research based on the existing literature (include references). Describe relevant prior experience and gaps in current knowledge. Describe any relevant preliminary data. Explain the significance of the research in terms of why it's important and how it will add to existing knowledge.*): Chronic kidney disease (CKD) is a major public health problem with over 19 million adults in the US diagnosed with early CKD and 640,000 adults with end stage renal disease (ESRD) [1-5]. Currently, CKD is staged based formulas derived by creatinine values. Limitations of such measures include confounding factors such as age, race and muscle mass. Acute kidney injury (AKI) on the other hand is an abrupt deterioration in renal function with or without reduced urine output. Using lab values to distinguish acute and chronic kidney disease can be impossible even to the trained physician, however their pathogenesis and treatment are different highlighting the need for an accurate diagnosis. Fibrosis is the common final pathway of CKD, with the degree of fibrosis directly related to severity [6, 7]. Acute processes on the other hand lead to inflammation or tubular dysfunction in the absence of fibrosis. Until now, the gold standard for diagnosing intrinsic kidney disease remains to be a biopsy. Kidney biopsies are usually indicated when pre renal or post renal causes of AKI have been excluded and a cause of the intrinsic renal dysfunction remains elusive. However, kidney biopsies are not without their disadvantages which include cost, risks related to its invasive nature and sampling error [8-11]. There are also instances, such as the acutely ill patient or those with bleeding tendencies, when a biopsy is contraindicated.Therefore, it seems prudent to develop a non-invasive marker for kidney fibrosis that would aid clinicians to decide about the need to obtain a biopsy. This is the premise of our research project, to determine whether shear wave elastography can be a reliable marker for kidney fibrosis.

Shear wave elastography (SWE) is an emerging technique which permits the non-invasive measurement of tissue elasticity [12]. This technique is now FDA approved for use in liver disease due to its ability to discriminate normal and cirrhotic liver tissue. Similar techniques have been investigated with varied success in other tissues including breast, thyroid and prostate. Studies of SWE have been performed on transplanted renal allografts showing an association between tissue stiffness measured by SWE and kidney fibrosis [13-15]. Transplanted kidneys are more superficial compared to native kidneys; thus estimates of tissue elasticity of transplanted allografts may not apply to native kidneys [16, 17]. Only few studies examined SWE in native kidneys and those had inherent limitations [18-20]. The main limitation being, there was no matchup between kidney fibrosis scores and SWE values. We propose to replicate the studies performed on transplanted kidneys while building upon and improving on the limitations of the prior studies conducted in native kidneys.

Kidney biopsy remains the gold standard for evaluation of kidney fibrosis in patients with abnormal kidney function. However, this invasive procedure is associated with: cost, risk of bleeding, infection, patient discomfort and sampling error. In other scenarios where patients are acutely ill, on anticoagulation or with very low platelet counts biopsies are in-fact contraindicated. SWE as a non-invasive marker of kidney fibrosis has the potential to provide immediate results at little cost with no harm to the patient. It will also likely reduce the rates of unnecessary biopsies and eliminate the complications associated with such an invasive procedure.

SWE is a novel FDA approved technique to assess organ fibrosis. Its successful application in the hepatology community has raised interest about its utility in other organs. We hope to extend the utility of this technique and use it in native kidney disease. Our study's goal is to determine whether SWE can be used as a non-invasive marker of kidney fibrosis. This study may have great clinical ramifications as the field of nephrology is expanding towards the development of non-invasive markers of kidney disease. The results of our study would provide clinicians with a tool that rapidly assesses tissue fibrosis while limiting the need for invasive and risky procedures. . Given the clinical and scientific need for this type of research, background of the investigators, identified population and potential for multiple future avenues of research, this project is important, novel, feasible and an excellent use of research resources.

4) Setting of the Human Research:

a. Indicate all AEHN locations where the human research will be conducted (check all that apply):

☒ Tabor Rd campus
☐ Elkins Park campus
☐ Belmont Center for Comprehensive Treatment
☐ Center One
☐ Montgomery campus
☐ Other: please specify -

b. Indicate if human research will be conducted at external location(s) overseen by the AEHN investigator (e.g. private physician office, collaborating hospital/university)

☐ Yes (Complete Appendix B: External Site Approvals on Application for Human Research)

☒ No

5) Resources available to conduct the Human Research:

a. Target population (e.g. Adult subjects with a diagnosis of Type II diabetes for greater than two years":
Adults over the age of 18 who underwent native kidney biopsy at the Einstein Medical Center in Philadelphia will be eligible for the study

b. **For prospective studies:**

i.) Total number of subjects planned to be enrolled in the study at AEHN site(s): 40

ii) For multi-site projects, please indicate total number of subjects planned to be enrolled in the study at all sites: N/A

iii) Describe access to a population that would allow recruitment of the targeted number of subjects (***i.e. how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?)*** : A list of patients who recently underwent a native kidney biopsy will be obtained from the pathology department on a weekly basis. Our research team will then contact the patients and discuss participation in the project. If they agree, during a follow up visit with the nephrologist formal informed consent will be obtained and questions answered. On a yearly basis, 50-60 native kidney biopsies are performed at AEMC. Therefore, we will need to recruit 80-90% of those patients.

Telephone script: Hello. My name is Dr " " and I am a medical doctor at the Albert Eisntein Medical Center. I am calling you with regards to a study we are conducting at our center involving a new ultrasound technique called shear wave elastography. We are recruting interested subjects who have had a kidney biopsy. You are qualified to participate in the study. If you are interested, your nephrologist will discuss the details of this study with you in greater detail during your follow up visit. Thank you and have a wonderful day.

c. **For retrospective studies:**

i.) Estimated number of charts to be reviewed: N/A

ii.) Time period of interest for data being collected **(e.g. *Subjects who had XX procedure between 6/1/00 and 6/1/05*:**

d. Describe the number and qualifications of the study team members, their experience in conducting research, their knowledge of the local study site(s), culture, and society: The study team members include 3 PGY2 residents, 1 PGY4 resident with prior research experience in this field, 1 PGY intern with interest in nephrology, 1 radiology resident PGY3, 1 radiology attending with experience in ultrasound imaging (director of body ultrasound at AEMC) and 1 nephrology attending with vast clinical and research experience.

e. Describe the time that the investigator and other study team members, if applicable, will devote to conducting and completing the study within the anticipated study period ***(e.g. 10% of PI's time and full-time coordinator)***: 80% of the PGY1 research half day will be used to conduct the study. Additional time may be required afterwards, in which case 10-20% of residents' time will be used to complete the study.

f. Describe the plan for ensuring that all investigators/staff assisting in this research are adequately informed of: 1) the protocol, including revisions to protocol and other study specific changes, 2) investigational product information if applicable, and 3) study related duties and functions: Regular meeting will be held to ensure all participants are on the same page. All members will be informed of changes to the protocol or study.

g. Describe the facilities available to conduct this research: The patients will undergo shear wave elastography imaging at the radiology department using the latest equipment to conduct such testing. This will take place at the AEMC. We will also use AECIS to access pathology reports and patients' demographics.

h. If applicable, describe the availability of medical or psychological resources that subjects might need as a result of the anticipated consequences of this research: Written and informed consent will be obtained from all the patients. In order to ensure the subject's understanding, they will be given the opportunity to ask as many questions as necessary. Furthermore, the consenting team will use "teach back" to assess the subjects understanding of the study's purpose and protocol.

6) Study Design

a. Recruitment Methods:

i. Describe when, where, and how potential subjects will be recruited (***Describe the source of subjects. Describe the methods that will be used to identify potential subjects. Describe materials, such as advertisements, that will be used to recruit subjects (include these with submission materials. If study is a chart review, describe which records will be accessed to collect data and how you will access them*** **:** A list of patients who recently underwent a native kidney biopsy will be obtained from the pathology department on a weekly basis. Our research team will then contact the patients and discuss participation in the project. If they agree, during a follow up visit with the nephrologist formal informed consent will be obtained and questions answered

ii. Will payments to subjects be provided?

☒ Yes, amount and timing: 25$ (cash) at the visit for the shear wave elastography measurements
☐ No
☐ N/A

b. Inclusion and Exclusion Criteria:

i. Describe how you will screen for eligibility (**e.g. review charts, perform specific screening tests, etc.**): Adults over the age of 18 who underwent native kidney biopsy at the Einstein Medical Center in Philadelphia will be eligible for the study

ii. Describe the criteria that define who will be included or excluded in your final study sample: Patients will be excluded for the following conditions:

- BMI > 35
- Patients with polycystic kidney disease, renal cell carcinoma, hydronephrosis or renal stones.
- Patients who develop severe post biopsy complications (infection, significant bleeding requiring transfusion or intervention)
- Pregnant patients.

c. Study Timelines:

i. Duration of an individual subject's participation in the study: 2-3 months

ii. Time period anticipated to enroll all study subjects or to complete chart review: 9 months

iii. Estimated overall study duration (***i.e. from initiation to completion of primary analyses***): 12 months

d. Study Endpoints:

i. Describe the primary and secondary study endpoints (***i.e. the outcome(s) that the study is designed to evaluate***): The primary outcome measure of this study is to determine whether tissue elasticity determined by SWE can assess kidney fibrosis.

ii. Describe any primary or secondary safety endpoints (***e.g. any disease or symptom that would result in the withdrawal of that subject from the study***): N/A

e. Human Research Methods:

i. Describe and explain the study design ***(e.g. randomized, double-blind, placebo-controlled clinical trial or retrospective chart review)***: Prospective cross-sectional study.

ii. Describe all research activities involved in this protocol, including a study visit timeline if appropriate: We will collect data on consecutive patients with the aim to have 10 patients in each fibrosis group (0-3). After consent, patients will be scheduled to come for a renal ultrasound and SWE. SWE examination will be conducted using an ultrasound machine equipped with a Philips Epiq ARFI Shear wave ElastPQ C1-5 mHz transducer. Shear wave

velocity will be obtained and an estimate of tissue elasticity (Young's modulus) will be calculated. All measurements will be performed by one of two qualified radiology physicians who will be blinded to the clinical and pathological data. We will allow a period of 90 days to obtain the images after the biopsy; otherwise the patient is no longer eligible to participate.

iii. Identify which tests/procedures are being administered solely for research purposes and which are being conducted as part of standard of care (i.e. procedures that would be done even if the participant were not involved in research): A renal ultrasound will be done as standard of care prior to any kidney biopsy. The shear wave elastography measurement will be done for research purposes.

iv. Describe steps taken to lessen the probability or magnitude of risks associated with tests/procedures being done for research purposes only (***e.g. only appropriately trained personnel involved in procedures, extra tests being done for safety purposes***): The shear wave elastography testing is harmless and painless with no implications on patients. Zero radiation exposure.

v. Describe alternative treatments that are available to subjects if they choose not to participate in research: N/A

vi. Describe the source records that will be used to collect data: AECIS will be used to obtain demographic data about the patients as well as laboratory values.

vii. Describe what data (variables) will be collected for this research: Baseline demographic information (Age, gender, race, height, weight, BMI), past medical history (Hypertension, heart failure, Diabetes Mellitus, Cerebrovascular accidents, dyslipidemia, hyperparathyroidism, coronary artery disease, peripheral vascular disease) laboratory data (serum electrolytes, complete blood count), kidney length and depth measurements as well as biopsy results will be obtained from the electronic medical record. Shear wave velocity will be obtained using a Philips ultrasound transducer and an estimate of tissue elasticity (Young's modulus) will be calculated. Use of any potential nephrotoxic medication will be noted including but not limited to: diuretics, Non-steroidal antiinflammatroy drugs, Angiotensin converting enzyme inhibitors / Angiotensin receptor blockers.

viii. Describe any plans to conduct audio or video recording of research participants during the conduct of the research. Specify whether recording is optional or not and how information on how recordings will be used and how long they will be retained is being shared with subject: N/A

f. Specimen Management:

i. Will any type of specimen (e.g. blood or tissue) be collected for this study?

☐ Yes
☒ No , skip to section on Data Management

ii. What information will be associated with the specimens collected for this study?

iii. If specimens will be banked for future use, describe where and how the specimens will be stored:

iv. Specify how long specimens will be stored locally:

v. Specify who will have access to the specimens locally:

vi. Will specimens be sent out or received: ☐ No ☐ Yes

a. Who is responsible for receipt or transmission of the specimens?

b. How will specimens be transported?

c. Describe the procedures to release specimens, including: the process to request a release, approvals required for release, who can obtain specimens, and the data to be provided with specimens:

g. Data Management

i. Describe steps that will be taken to secure the data (e.g. training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality and separation of identifiers and data) during storage, use and transmission: A master list of MRNs of patients meeting the criteria will be composed. Each patient will then be assigned a study ID number. All information will be tabulated and kept as a data collection file which will not contain identifiers. All eligible patient data will be numbered and analyzed. The information will be stored on a secure HIPPA compliant folder on an Einstein computer as a password protected file. Upon completion of all necessary information on file, the master list with identifiers will be deleted.

ii. Describe the data analysis plan, including any statistical procedures and method for determining the sample size for the study: Descriptive statistics will be used to summarize the patient characteristics. Data for continuous variables will be presented as mean + SD and categorical variables as numbers and percentages. Linear regression analysis will be performed to describe the relation of the extent of fibrosis and parenchymal stiffness. Stiffness values of patients with different fibrosis grades will be compared using the Mann-Whitney U-test. Statistical analyses will be performed using JMP version 9.0 (Cary, North Carolina, USA).

iii. Describe where and how data will be stored locally: Data will be stored on a shared drive as a password protected file with access only to members of the research team.

iv. Specify how long data will be stored locally: 6 years.

v. Specify who will have access to the data locally: Participants in this research project only

vi. Describe process that will be followed to ensure accuracy of collected data: Renal ultrasound and shear wave elastography measurements will be performed by an experienced radiologist with over 10 years of ultrasound imaging experience.

vii. Will data be sent out or received: ☒ No ☐ Yes

a. Who is responsible for receipt or transmission of the data? N/A

b. How will the data be transported? N/A

h. Provisions to monitor the data for the safety of subjects (Required only when Human Research involves more than minimal risk):

i. Describe plans to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe. Include what data will be reviewed, who will review the data and when the data will be reviewed: Baseline demographic data, laboratory results, SWE measurements and biopsy results will be aggregated into an encrypted study database; all data will be checked twice upon entering it into the database to ensure accurancy. The data will be checked and updated by the primary and co-investigators on a weekly basis.

i. Withdrawal of Subjects:

i. Describe the anticipated circumstances under which subjects will be withdrawn from the research without their consent: Patients are fully entitled to decline in participating in the study. They will only have undergo a renal ultrasound and shear wave elastography measurement on one occasion and will not be required to follow up with us afterwards.

ii. Describe the procedures that will be followed when subjects withdraw from the research (or request that their data be withdrawn), including partial withdrawal from procedures with continued data collection: Patients who chose not to participate will have their data deleted / removed from the data base.

7) Risks to Subjects:

a) List the reasonably foreseeable risks, discomforts, hazards or inconveniences to the subjects. For each indicate the probability, magnitude, and duration when possible (consider physical, psychological, social, legal and economic risks as well as risks related to confidentiality): Risk of violation of confidentiality. To minimize the risk: password protected list of patients accessible only to members of the research team. In terms of the ultrasound measurements, the Gel used to improve visualization is cold and causes very mild discomfort but no pain.

b) If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable: N/A

c) If applicable, indicate which procedures may have risks to an embryo or fetus should the subject or the subject's partner be or become pregnant: N/A

d) Describe, if applicable, the process that will be followed if a subject or the subjects' partner becomes pregnant while participating in the study: N/A

e) If applicable, describe risks to others who are not subjects: N/A

8) Potential Benefits to Subjects

a) Describe the benefits that individual subjects may experience (include when possible the probability, magnitude and duration of the potential benefits) or indicate if there is no direct benefit: The subjects will not benefit. However, determining whether shear wave elastography measurments can predict the degree of fibrosis in diseased kidneys can be of great clinical significance. This may reduce the rates of unnecessary biopsies and eliminate the complications associated with such an invasive procedure.

9) Medical care and compensation for injury (Required for Greater than Minimal Risk Studies Only):

a) Describe any provisions for medical care and available compensation in the event of a research related injury: N/A

b) Provide the contract language, if any, relevant to compensation for research-related injury: N/A

10) Cost to participants:

a) Describe any actual or potential cost that subjects may incur through participation: N/A

11) Provisions to Protect the Privacy Interests of Subjects:

a) Describe the steps that will be taken to protect the subjects' privacy interests and make them feel at ease. In this case, "privacy interest" refers to a person's desire to control access of others to themselves (*e.g. has consideration been made to having same gender interviewers, the disclosing of cameras, conducting physical exams in private rooms, discussing study health concerns of subjects in private rooms instead of public waiting areas, etc.*): Discussion of the study details in private/ physician consultation rooms. The ultrasound diagnostic studies will be undertaken in a private radiology room.

12) Subject Authorization

Are you planning to obtain written HIPAA authorization from study subjects?

☒ Yes
☐ No (if checked, written approval for waiver from Privacy Officer is required)

13) Consent process:

a) Indicate the type of informed consent you propose to utilize in this research project:

☐ Requesting Waiver of Consent Process

Provide justification for why it would not be practicable (feasible) to conduct this research without a waiver:

Explain whether or not subjects will be provided with additional pertinent information after their participation and if yes, describe what information will be provided and how it will be communicated (*e.g. a summary of study results will be provided to subjects in a newsletter*): N/A

SKIP TO SECTION 14

☐ Requesting an Alteration to the Consent Process (i.e. no documentation in writing)

Provide details on alteration requested (***e.g. only verbal consent will be obtained, required information will not be disclosed or the research involves deception***) and why it is necessary:

☒ Consent process with Documentation in Writing

b) Describe when and where the consent discussion will take place: Our research team will contact the eligible patients and discuss participation in the project. If they agree, during a follow up visit with the nephrologist formal informed consent will be obtained and questions answered.

c) Describe the role of the individual(s) involved in obtaining consent from study subjects **(e.g. investigator, study coordinator, recruiter, etc.)**: The primary nephrologists will sit down with the patients and explain the study details to the individuals. They will be allowed time to ask questions.

d) Specify the time that will be devoted to the consent discussion: 10 minutes. Patients are also allowed to contact the investigators for further information / clarification.

e) Will subjects be given the opportunity to think about the information provided as part of the consent discussion, ask questions, and discuss the research with family or friends if desired?

☒ Yes
☐ No

f) Describe the steps that will be taken to minimize the possibility of coercion or undue influence:
Patients will receive a phone call about the study participation. If they are interested they will have sufficient time to think about the study participation until they meet the nephrologist for their follow up

meeting. During the consultation and if the patient decides to participate, the study will be explained including risks/benefits that will allow to the patient to reach an informed decision.

g) From whom will consent or permission for research participation be sought (i.e. subject, parent, legally authorized representative): subjects/patients themselves.

h) Describe process to ensure subject/parent/LAR's understanding: Written information will be provided to the patient as well as a verbal explanation of the project.

i) Do you plan to consent subjects or their legally authorized representatives when the subject does not speak English?

- ☒ Yes
- ☐ No

If yes, select one of the two options below that best describes your study:

- ☐ The research targets a specific population that is non-English speaking OR a significant proportion of subjects are anticipated to be non-English speaking (*if this is true, translations of the standard (i.e. IRB-approved, full-description) informed consent documents must be reviewed and approved by the IRB prior to enrollment of any non-English speaking subjects*).
- ☒ The research does not target a non-English speaking population, AND only a small proportion of subjects are anticipated to be non-English speaking (*if this is true and a translated study consent form is not available, the short form consent process must be used. For more information, see the Investigator Manual*.)

Describe your plan for conducting study visits and long-term follow-up with these subjects: Patients will be consented using the help of a translator line / person. benefits and risks will be explained in detail. Reliable contact information will be obtain (cell phone number) in order to reach the patient in the future.

j) Does the study allow for and do you plan to enroll adult participants with diminished decision making capacity?

- ☐ Yes
- ☒ No

If yes, select one of the two statements in each group below that is most appropriate for your study (if neither statement applies in one or both groups, your study does not meet the regulatory criteria for enrollment of these subjects):

Criterion 1(*must select one box below if you plan to enroll adults who are unable to consent for themselves*):

- ☐ The aims of the research cannot be accomplished if the subjects were limited to adults capable of consent.
- ☐ The research is intended to be beneficial to the subjects in a manner that is not available outside the research context.

Criterion 2 (*must select one box below if you plan to enroll adults who are unable to consent for themselves*):

- ☐ The research involves no more than minimal risk to subjects. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life of normal persons or during the

performance of routine physical or psychological examinations or tests in normal persons [45 CFR 46.102(i)].

☐ The research involves more than minimal risk to subjects, but the research holds out the prospect of direct benefit to the individual subjects.

☐ The research involves more than minimal risk to subjects, there is no anticipated direct benefit to the individual subjects, but: (1) the subjects have a disease or condition for which the procedures involved in the research are intended, (2) foreseeable risks to the subjects are low AND (3) the negative impact on the subject's well-being is minimized and low.

Describe your plan for assessing a potential subject's ability to provide informed consent (e.g. clinical interview, standardized psychological or neuropsychological test, specially developed capacity assessment instrument, etc.):

14) Vulnerable populations:

a) Indicate if any individuals who are potentially vulnerable to coercion or undue influence will be included in the study:

- ☐ Children (if checked, must complete Appendix C. Children on Application for Human Research)
- ☐ Pregnant Women
- ☐ Neonates of Uncertain Viability or Non-viable Neonates
- ☐ Prisoners
- ☐ Adults with Diminished Decision Making Capacity
- ☐ Students/ Employees

***You may not include members of the above populations as subjects in your research unless it is indicated in the inclusion criteria of the protocol and approved by the IRB.**

b) If vulnerable populations will be participating in the study, describe the rationale for including this population and the additional safeguards to protect their rights and welfare: N/A

c) If research involves children, describe the following:

i. Will parental permission be obtained from either both parents or just one parent: N/A

ii. Will assent be obtained from all, some, or none of the children? If assent will be obtained from some children, indicate which children will be required to assent: N/A

iii. When assent of children is obtained, describe whether and how it will be documented: N/A

15) Is this Community-Based Participatory Research (*i.e. research conducted in communities in which community members, persons affected by condition or issue under study and other key stakeholders in the community's health have the opportunity to be full participants in each phase of the work including conception, design, conduct, analysis, interpretation, conclusions, and communication of results*):

- ☐ Yes
- ☒ No, go to section 16)

Describe involvement of the community in the design and conduct of the research:

16) Sharing of results with participants:

a) Describe any plans for sharing results with participants: All patients will receive a written layman summary about the results of the study if they are interested.

If separate protocol is not included, please attach list of references for background section etc. to this form.