Request of funds for the development of:

An inexpensive handheld ultrasound-based device for the detection of liver fibrosis

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Grant Proposal Submitted to the Vanderbilt University School of Engineering
Proposal Narrative

I. Executive Summary
   Not applicable at this time

II. Problem Statement and Objective
   Although the exact number of people worldwide who are affected by liver cirrhosis is unknown, it has been estimated at 400,000 in the United States, accounting for over 25,000 deaths. In Africa and Asia, numbers are even higher due to the prevalence of hepatitis B and C. The current gold standard for diagnosing liver cirrhosis is liver biopsy, however this method has several shortcomings including invasivity and sampling variability due to tissue inhomogeneity[1].

   Ultrasound elastography is a promising new technique for the noninvasive diagnosis of liver fibrosis and cirrhosis. At the moment, however, this method is considered suboptimal, particularly in diagnosis of intermediate stages of the disease [2]. Recent progress in MR and ultrasonic imaging has shown promise of an effective technique for diagnosis, but this method is currently too expensive for implementation in most places. Measurement sensitivity in the early stages of disease is also a concern of this technique [1]. The purpose of this work is to engineer an ultrasound-based device to noninvasively diagnose liver fibrosis and cirrhosis.

III. Documentation of Final Design
   Not applicable at this time

IV. Prototype of Final Design
   While we do not have a final design constructed at this juncture, the team on this project last year was attempting to construct a single piston ultrasound transducer prototype that displays clear RF data. This data can be passed through algorithms developed by Dr. Byram and his lab to generate tables that correlate RF time to peak displacement in order to detect the stages of liver fibrosis. Figure 1 shows a block diagram of what the previous team was trying to accomplish.
   The previous team was able to develop the Transmit/Receive switch and make progress on the buffer amplifier and the low noise amplifier for the system. Our team plans to assess this progress and if it is viable, attempt to continue where they left off.

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Figure 1. Block diagram of system prototype.
V. **Proof of Functionality**

Liver stiffness measurements have been shown to be well correlated with the range of fibrosis stages thus elastography theoretically could be a viable tool in measuring the extent of cirrhosis.[3]

VI. **Related Products and Patents**

*Vscan:* The Vscan is a portable ultrasound device created by GE Healthcare. Unlike our proposed design, it is not a single-purpose ultrasound; rather, it is a qualitative ultrasound that provides image data as opposed to quantitative data. While we do aim to have a similar level of portability, our design will be created with a single-element array that only provides a stiffness measurement. In addition, the Vscan currently costs $7,900. While reducing cost is only one of the goals of this project, we hope to have an end product that is significantly less expensive due to its decreased complexity.

*MobiUS SP1:* The MobiUS SP1 is a smartphone ultrasonic device created by MobiSante. It is notable in that it is portable and can allow for 90 minutes of scan time on a full charge (increasing the portability aspect). However, like the Vscan (and unlike our proposed device), it provides qualitative image data as opposed to quantitative stiffness data.

US 20150148671 A1: This patent refers to a liver fibrosis diagnostic device created at National Taiwan University. While this device and our design share similar characteristics in that both utilize single element arrays to quantify liver fibrosis, they differ in detection mechanism. While our design utilizes the Bayesian reconstruction algorithm to analyze data, theirs uses correction for the Nakagami factor. Additionally, this device lacks the portability that we aim to include.

Other ultrasonic devices exist that have similar aspects to our proposed device, but they are either 1) not portable, or 2) do not provide quantitative data.

VII. **Anticipated Regulatory Pathway**

We anticipate that our proposed device will qualify to enter the 510k pathway for FDA approval. A similar product, the MobiUS SP1 discussed in VI.A, was able to enter the 510(k) approval process as a Class II medical device [4]. As our device is similar in functionality and risk, we anticipate that the approval process will be the same.

VIII. **Reimbursement**

Since the primary use of our device will be in low-resource environments on a global scale, we recognize that the relevance of reimbursement by Medicare and Medicaid coverage may not be applicable. However, when used in the United States, we expect that our device will be reimbursable by the Centers for Medicare and Medicaid Services (CMS). We anticipate that our device will qualify for 510(k) regulatory clearance by the FDA, which increases the likelihood of reimbursement [5] since other ultrasound devices have received CMS coverage. To maximize our device’s chances of being reimbursable, we will employ device testing modeled after well-designed comparative clinical trials to substantiate the medical benefit and added value of our device. Meeting these two requirements and showing comparable efficacy of our device in
relation to other 510 (k) ultrasound devices should qualify our device for reimbursement. Furthermore, given how the average age for liver cancer diagnosis is 63 years old [6], our device will likely be used for assessing liver fibrosis in many older patients. This makes our device more likely to qualify for Medicare reimbursement.

IX. Anticipated Manufacturing Costs

Estimated cost per unit device. Because the design has not been finalized we were not yet able to estimate complete manufacturing cost.

Table 1. Expenses Breakdown

<table>
<thead>
<tr>
<th>Expense</th>
<th>Estimated Cost</th>
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<tbody>
<tr>
<td>Transducer</td>
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</tr>
<tr>
<td>Circuit Board</td>
<td>$20</td>
</tr>
<tr>
<td>Amplifiers</td>
<td>$80</td>
</tr>
<tr>
<td>Monitor</td>
<td>$200</td>
</tr>
<tr>
<td>Teensy/Arduino</td>
<td>$40</td>
</tr>
<tr>
<td>Total</td>
<td>$940</td>
</tr>
</tbody>
</table>

X. Potential Market

The ultimate target for this device will be care facilities in low resources areas of the developing world. Thus, a primary goal is to make the product low cost, so that it will be a viable resource in these areas. Another potential market for this product, however, is right here in the US and other developed nations in which this device can be implemented into hospitals. Currently the process to be screened for liver fibrosis involves a great deal of scheduling between multiple departments in the hospital in order to get access to proper equipment. The patient must come in on a separate occasion to be tested in a different department, wasting time, energy, and money. By making our device directly available to primary physicians, testing can be performed immediately and on site at the primary appointment. This will save both the patient and the hospital time and money and enable a smoother, more efficient process. Our final product will thus be marketable to both established hospitals, as well as those in the developing world.

XI. Team Description

There are six members on our team. Lauren Severance has done research with focused ultrasound using phantom materials. She also has research experience in MR image processing. Sara Keller has done MR image processing and has experience in finite element modeling. Patricia Twilley has done research in focused ultrasound using phantom materials. Meredith Huszagh has extensive experience shadowing doctors and will be an excellent source of information when considering the patient experience involved in our device. Alison Williams has taken a medical imaging course and has significant Matlab programming experience from her
undergraduate research. Fahad Iqbal has taken a special topics course in ultrasound imaging. All team members have experience in biomedical instrumentation, circuit design, and Arduino programming. Four members, Lauren, Sara, Patricia, and Alison, worked together last spring on the development of a smart pillbox using the Arduino platform.

References