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TITLE: Clinical Study of Vascular Plaque Determination for Stroke Risk Assessment

PRINCIPAL INVESTIGATOR: D. Geoffrey Vince, PhD.

CONTRACTING ORGANIZATION: The Cleveland Clinic Foundation, Cleveland, OH

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**6. AUTHOR(S)**
D. Geoffrey Vince
Russell J. Fedewa
Sheronica L. James

E-Mail: vinceg@ccf.org

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Cleveland Clinic Foundation, The
9500 Euclid Avenue
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**14. ABSTRACT**

The high rate of diabetes for the veteran population (~20%) tracks with high rates of obesity and these both have increased complications that include carotid stenosis and risk of stroke. Composition information is not available for carotid stenosis even though it is a more import predictor of stroke risk than degree of stenosis. Our hypothesis is that there exist correlations between the information provided by the **C**ompositional **A**nalysis **S**ystem by **M**achine learning (CASM) algorithm and future outcomes for patients with carotid artery stenosis. This research effort involves enrolling up to 1500 subjects with significant carotid stenosis at two sites. The asymptomatic patients are followed for up to 3 years in order to determine if there are correlations between future risk of stroke and the output of the CASM algorithm. In addition the output of the CASM algorithm will be analyzed for key populations: e.g. diabetic vs non-diabetic and asymptomatic vs symptomatic. **The first subject has been enrolled at each site.**

**15. SUBJECT TERMS**
diabetes, atherosclerosis, stroke, carotid stenosis, cerebrovascular accident, ultrasound, spectral analysis, tissue characterization, machine learning

| **16. SECURITY CLASSIFICATION OF:** | | | **17. LIMITATION OF ABSTRACT** | **18. NUMBER OF PAGES** | **19a. NAME OF RESPONSIBLE PERSON** |
|---|---|---|---|---|---|
| **a. REPORT** | **b. ABSTRACT** | **c. THIS PAGE** | | | USAMRMC |
| Unclassified | Unclassified | Unclassified | Unclassified | 20 | **19b. TELEPHONE NUMBER** *(include area code)* |

## TABLE OF CONTENTS

## 1. INTRODUCTION:

Higher rates of diabetes in the veteran population is a contributing factor in the higher rates of carotid stenosis and subsequent stroke as compared to the general population. Currently, the degree of stenosis is a key determinant in the recommended course of treatment for carotid plaque, but this measure is blind to the risk arising from composition which is not clinically available. To address this need for composition information, the Compositional Analysis System by Machine learning (CASM) algorithm was developed based on spectral analysis of backscattered ultrasound to provide a noninvasive measure of carotid plaque composition. This research effort is designed to determine correlations between output from the CASM algorithm and future outcomes regarding stroke for patients with carotid stenosis. To accomplish this, a prospective longitudinal clinical study is currently being run to enroll 1500 subjects at two sites. Each enrolled patient receives a research ultrasound which provides input data for the CASM algorithm and if they are asymptomatic with no interventions involving their carotid, then they are followed for up to 3 years. The measurements from the CASM algorithm will be obtained and compared between diabetic and non-diabetic, symptomatic and non-symptomatic, and over time for asymptomatic subjects. These correlations will form the basis for a future clinical trial and 510k application to FDA.

## 2. KEYWORDS:

Diabetes, atherosclerosis, stroke, carotid stenosis, cerebrovascular accident, ultrasound, spectral analysis, tissue characterization, machine learning

## 3. ACCOMPLISHMENTS:

- **What were the major goals of the project?**

  This research project, *Clinical Study of Vascular Plaque Determination for Stroke Risk Assessment*, contains six mayor tasks in order to achieve the three specific aims. The clinical study at the heart of this research effort has two sites: The Cleveland Clinic Foundation (CCF) and the Cleveland VA Medical Research and Education Foundation (VA).

**AIM 1:** Determine the Correlation between Ultrasonically Obtained Plaque Composition and Future Cerebrovascular Accident (CVA)

**Major Task 1: Obtain major equipment and regulatory approval**

- Update legal documents with Seimens (***goal: month 1***):
  **Completed** prior to the start of the contract.

- Obtain two modified research ultrasound machines from Siemens (***goal month 1***)
  - *Milestone*: Ultrasound system hardware delivery:
    - CCF: **Completed** prior to the start of the contract.
    - VA**:** **Completed** Month 8

- Final Software Installation for Research Ultrasound Exam from Siemens:
  - CCF: **Completed** Month 7
  - VA: **Completed** Month 8

- *Milestone*: Local IRB Approval (***goal month 3*****)**
  - CCF: **Completed** Month 9**:** 11 Jun 2021
  - VA: **Completed** Month 9**:** 10 Jun 2021
- *Milestone*: HRPO Approval (***goal month 6***)
  - CCF: **Completed** Month 12**:** 19 Aug 2021
  - VA: **Completed** Month 11**:** 30 Jul 2021
- *Milestone*: Complete 510k Application (***goal month 48***):
  - Plan to complete in September 2024.

**Major Task 2: Fabricate plaque volumetric determination system**

- Procurement of hardware and fabrication of device (***goal month 1***)
  - Procurement of hardware: **Completed** Month 1: 2 Oct 2021
  - Fabrication of Device: **Completed** Month 6: 17 Feb 2021

- *Milestone*: Creation of control software and integration with ultrasound system (***goal month 2***)
  - **Completed** Month 10

**Major Task 3: Enroll patients for Aim1, 2, and 3**

- Start Enrollment **(goal month 6):**
  - CCF: **Completed** 15 Sep 2021
  - VA: **Completed** 10 Sep 2021
- *Milestone*: Reach 1500 Enrollment for Study **(goal month 36)**
  - CCF: 900 **0.1%** completed
  - VA: 600 **0.2%** completed

**AIM 2:** Does the Presence of Diabetes Affect Estimate of Carotid Plaque Composition?

**Major Task 1: Determination of vascular geometry and composition**

- Develop and test automated border detection algorithms
  **(goal: start month 5 and complete month 30)**
  - Subtask - Manual borders production **0.1%** completed: started in month 12
  - Subtask - Automated algorithm development: start in month 18
- Create plaque compositional images using the CASM software
  (task is repeated in SOW under AIM 2 Task 2 and AIM 3 Task 1)
  **(goal: start month 5 and complete month 48)**
  0.1% completed started in month 12

- *Milestone*: Geometry and composition of all vascular structures quantified
  0 % completed

**Major Task 2: Determine the effect of diabetes on carotid plaque composition**

- Identify diabetic patients and find matched controls
  **(goal: start month 36 and complete month 48)**
  - Start in month 36
- Create plaque compositional images using the CASM software
  (see above: same task as AIM 2 Task 1)
- *Milestone*: Statistical correlation between plaque composition and geometry between diabetic and non-diabetic patients produced.
  0% completed. Plan to start in month 37

**AIM 3:** Does Estimate of Plaque Composition Correlate with Future Changes in Plaque Composition

**Major Task 1: Determine the rate of plaque progression and correlate with risk factors and medication.**

- Identify all patients with baseline and follow-up data
  **(goal: start month 36 and complete month 48)** plan to start in month 36
- Use segmentation software to identify vascular borders
  **(goal: start month 30 and complete month 48)** plan to start in month 30
- Create plaque compositional images using the CASM software
  (see above: same task as AIM 2 Task 1)
- *Milestone*: Statistical correlation between plaque composition, geometry, and risk factors.
  0% completed. Plan to start in month 37

- **What was accomplished under these goals?**

  - **Clinical Study Enrollment**

  We achieved initial enrollment at end of the first year which was 6-7 months behind schedule. The primary source of delay was the unexpected effort in modifying the Siemens Sequoia ultrasound systems and safety testing.

  - **Ultrasound System Background**

  Under the prior research funding ("Vascular Plaque Determination for Stroke Risk Assessment", W81XWH-16-1-0608), our group developed the CASM algorithm based on using a Siemens S3000 ultrasound system with specific settings (see Table 1). A key to success in the current research is to collect ultrasound during the research ultrasound exam that has a comparable bandwidth to the S3000 system that the CASM algorithm is based on. After receiving news in December of 2019 that our proposal was chosen to be funded, we contacted Siemens to negotiate an extension on the agreement based on the

support letter that Siemens provided as part of this grant proposal. Siemens stated that their newest system, the Sequoia, would be able to capture data comparable to the S3000 and provide a greater total number of frames captured in one continuous acquisition which would enable the imaging of the entire plaque in one capture rather than multiple captures that were needed with the S3000. This improved ability would avoid the need to 'stitch' together different acquisition in order to perform a 3D reconstruction of the plaque. We agreed to work with the new system.

Another key difference between the S3000 and the Sequoia was in the transmit/receive design for image formation. The S3000 implemented a single transmit/single receive approach where a beam is transmitted on a subset of the elements in the transducer array. The backscattered signals from the tissue are then received by a subset of the elements and a single beam line is formed by adding up these received signals. This single line is then used to create a single line in the ultrasound image. The next line is formed by shifting transmitted beam along the array by choosing a slightly different sect of elements as the transmitting elements. In this manner a full image is created. The Sequoia, however, implemented a single transmit/multiple receive approach, which is a way to increase the frame rate while maintaining spatial resolution (see Table 1 for a comparison of frame rates) at the cost of greater signal processing requirements. The single transmit/multiple receive approach forms an image with fewer number of transmitted signals by combining receive lines from multiple transmits together into 'virtual' image lines and thus maintaining resolution. This type of approach is compatible with the CASM algorithm since it has no effect on the bandwidth of the backscattered ultrasound and it is the bandwidth that is critical for the CASM algorithm to work.

In October 2020, the initial FDA approved software from Siemens was installed on the Sequoia. This software did provide the ability to access received raw signals, but these signals required processing through proprietary software that Siemens was not willing to provide to the research team. Two approaches were proposed to solve this issue: (1) all raw signals would be collected and sent to Siemens for processing prior to be sent back for analysis or (2) modify the Sequoia to mimic the single transmit/single receive approach used by the S3000. The first option would require the creation of a secure data transfer apparatus and personnel time commitment on both sides, but would permit the use the FDA approved software. Both Siemens and our group considered this impractical on grounds of logistics and data integrity, especially considering that it would involve the potential sharing of PHI (i.e. dates) with Siemens. Thus we chose the second option which involved changing five settings in the software configuration files. Unfortunately, these changes were outside of the FDA approved use of the software. Making these changes seemed the most reasonable path even though it would invalidate the FDA approval, require safety testing by Siemens, and the protocol and informed consent would need to be modified (CCF IRB was reviewing the study at the time). An FDA approved machine was not required for the study since none of the research data was being used for clinical care. The key benefits were as follows:

1. Avoid the need to send all data to Siemens and back to CCF.

2. Permitted the fine tuning of the transmit and receive settings to match the bandwidth of the S3000 and thus the CASM algorithm can be applied without adaptation to a shared bandwidth between the two systems.

   Note: the CASM algorithm can be ported to a new system as long as the bandwidths are similar and identical bandwidths require no adjustment to the CASM algorithm. Only action needed is to take a new set of reference data with the Sequoia system using the same phantom as used for the S3000 reference data. The reference data are used to normalize the power spectra prior to extraction of spectral parameters. The spectral parameters are used as the input values for the CASM algorithm.

- **The Modified Sequoia Ultrasound System**

**Table 1:** Comparison of the S3000 settings used for the creation of the CASM algorithm with the default Sequoia settings and the modified Sequoia settings. The frame rate is heavily influenced by the number of transmit lines and is not affected by the number of receive lines. Modifying the Sequoia increased the bandwidth overlap from a slightly over 90% to effectively 100%.

| **Setting** | **S3000/CASM** | **Sequoia (default)** | **Sequoia (modified)** |
|---|---|---|---|
| Transmit Lines per frame | 456 | 120 | 456 |
| Lines per mm | 12.1 | 3.1 | 11.8 |
| Receive Lines per Transmit | 1 | 11 | 1 |
| Transmits per Transmit Position (Pulse Inversion for Harmonic Imaging) | 2 | 2 | 2 |
| Frame Rate (fps) | 14 | 40 | 12.5 |
| Pulse Repetition Rate (Transmits/sec) | 12,768 | 9,600 | 11,400 |
| | | | |
| *20 dB Bandwidth* | | | |
| Fundamental Low Frequency (MHz) | 2.5 | 2.2 | 2.5 |
| Fundamental High Frequency (MHz) | 6.9 | 6.5 | 7.0 |
| Harmonic Low Frequency (MHz) | 4.9 | 4.6 | 4.8 |
| Harmonic High Frequency (MHz) | 10.1 | 9.7 | 10.1 |

In December 2020, the changes to the configuration files on the Sequoia were finalized. The modified Sequoia passed the safety testing in April 2021 at Siemens. The exact reasons for the delay in safety testing at Siemens is not known even though we were in constant contact with the Siemens engineering team. In Table 1, the similarity can be seen between the S3000 and the modified Sequoia. Specifically, the bandwidths for both the Fundamental and nonlinearly generated second harmonic portions of the backscatter are effectively the same. The number of lines per frame are also the same, thus the regions of interest (ROI) for classification by the CASM algorithm will contain the same number of lines.

The CASM results from different locations within a uniform phantom (model 044, CIRS, Inc. Norfolk, VA) are shown in Figure 1. The left image is the result from the S3000, while the right image is the result from the modified Sequoia. We expect this phantom to most closely resemble fibrous tissue (thus the green shading). There are two ROI's that were classified as hemorrhagic or necrotic. This could be a misclassification or there

could be something different in the phantom at those positions since the S3000 and Sequoia data were not taken at the same places. This provides a visual check on the CASM algorithm applied to the modified Sequoia data and was an initial test of the software workflow for the CASM algorithm adopted to the Sequoia data set.

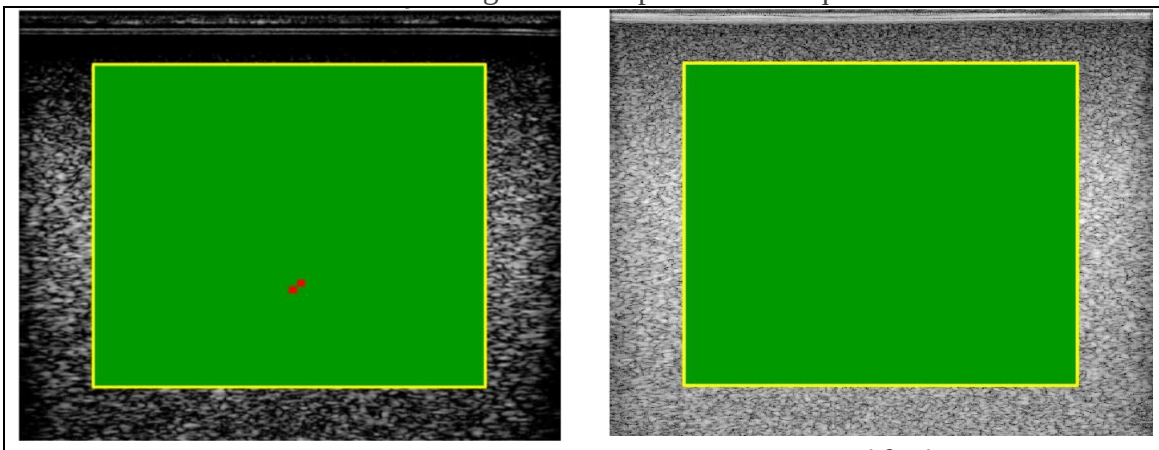



**Figure 1**: CASM algorithm results compared between S3000 and modified Sequoia. The expectation was that the tissue mimicking phantom would be classified as fibrous (green) which is true for all but two ROI's. Each image is 4cm deep and 38 mm wide.

- **Fabrication of Position/Orientation Tracking Hardware and Software for the Data Acquisition Process**

In order to track the relative position and orientation of the ultrasound probe, an inertial measurement unit (IMU) ) (vn-100 rugged from VectorNav, Dallas, TX) has been successfully mounted on the probe handle. A 3-D printed sleeve was designed and manufactured to hold the IMU in a set orientation as shown in Figure 2. The IMU cable is connected to a USB port on a laptop and data from the IMU is obtained via custom built software in Matlab (Mathworks, Natick, MA). The data acquisition procedure developed relies on the following steps:

1. Sync the computer clock of the laptop with the clock of the ultrasound system (see below for details)
2. Start collecting IMU data sets with laptop timestamp while holding probe still at proximal end of the plaque
3. Start collecting raw signals on the ultrasound system
4. Begin sliding the probe along the patients skin to image the entire carotid plaque in a transverse direction
5. Stop moving the probe when you pass the distal end of the plaque region. Hold probe still at distal end of the plaque until IMU data stops being collected.
6. Stop collecting raw ultrasound signals
7. Stop collecting IMU data.
8. Following this collection, color Doppler video loops at roughly half cm spacing are collected from proximal to distal ends of the plaque. Each video loop captures roughly three heart cycles of a single site. These series of videos aid the lumen border detection.

These steps are automated within Matlab software and the Ultrasound system so that a research tech presses one button to initiate the process and the sonographer presses two buttons immediately following and then begins to slide along the surface of the skin. The data collection steps are terminated by the respective software. Each collection is designed to run for slightly less than 10 seconds and collects 120 frames of data.

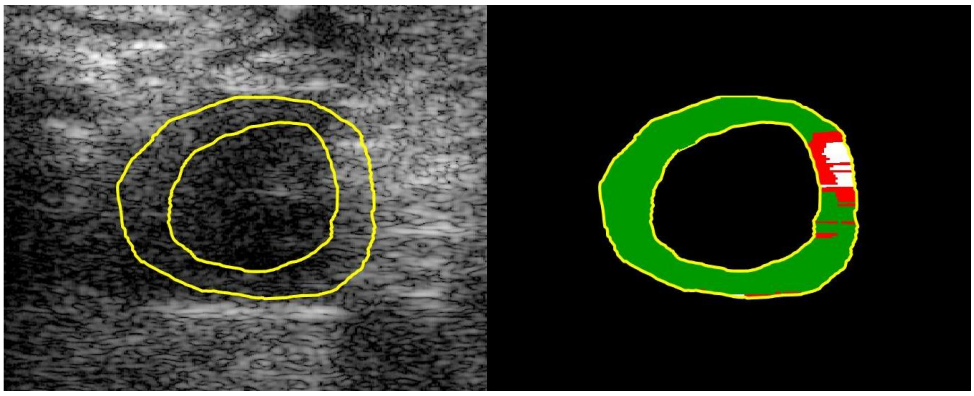
*Time Sync:* In order to perform 3D reconstruction of the segmented plaque, the computer clocks on the Sequoia and laptop must be synced. On the Sequoia, the set of raw signals for each frame are saved as a single file that contains the timestamp from the CPU clock on the Sequoia system. The Sequoia is not enabled to be externally triggered for this data acquisition or capable of sending out a trigger pulse at the start of a data acquisition. Thus we designed a method to sync the two systems based on the release of the software button that starts the ultrasound raw signal data acquisition on the Sequoia. Specifically, we used an off the shelf device designed to stream the image of a monitor output (Sequoia) into a window of a second computer (control laptop) with no time lag: Elgato HD60s (Corsair GmbH, Munich, Germany). Then custom code in Matlab was written to record the laptop CPU clock time when the button to begin data acquisition on the Sequoia is released. This provides a sync between the two with variability within the time of one ultrasound frame (i.e. 80 msec). These sync files are then archived with the raw data.


**Figure 2**: Mount for IMU on the 10L4 Sequoia ultrasound probe.

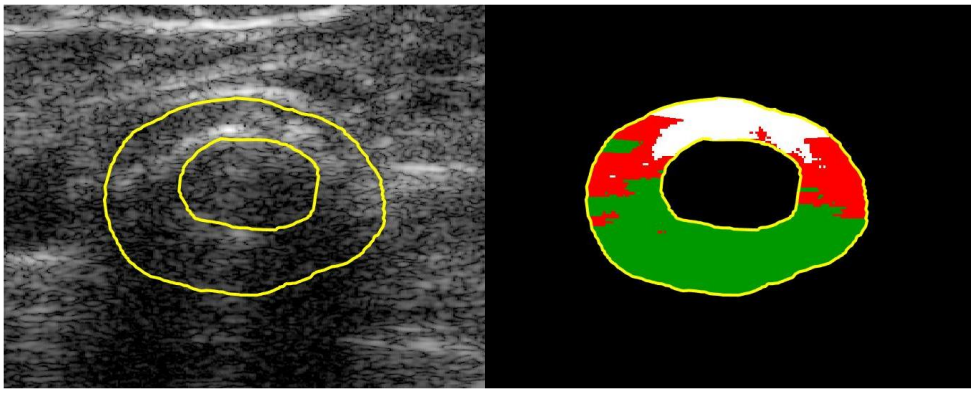
- **Image Segmentation**

To make the most of the delays in obtaining a research ultrasound system, the research team spent time working on manual image segmentation skills using data collected from the prior research effort that created the CASM algorithm. Within custom software in Matlab, the raw signals from the S3000 that were collected from human subjects in the prior study was converted into images and displayed so that the user could trace the lumen (i.e. blood-plaque boundary) and outer vessel (i.e. media-adventitial boundary). This tool has been adapted for processing the Sequoia data and loops with the ability to quickly move from frame to frame for the 120 frame loop acquisitions where the probe is swiped along the skin from the proximal end of the plaque to the distal end (data acquisition described above).

Proximal End of Plaque in Common Carotid Artery



Mid-Region of Plaque in Common Carotid Artery



Distal End of Plaque in Internal Carotid Artery

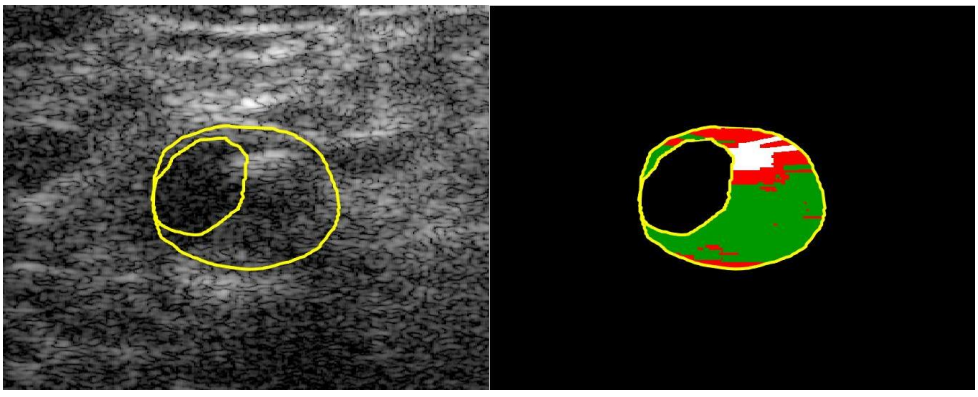


**Figure 3**: Sample CASM results from subject CC00001. Left column depicts the borders overlaid on the grayscale image, and the right column contains the CASM algorithm output. Green represents fibrous or fibro-fatty regions, Red represents hemorrhagic and/or necrotic core regions, and White represents calcified regions. Each image is represents a depth of 1.8 cm and a width of 2.1 cm. CASM applied with a 90% overlap for the ROI's. Green represents fibrous or fibro-fatty, red represents hemorrhagic and/or necrotic core, and white represents calcium.

For the first case collected at Cleveland Clinic, we have preliminary borders and have applied the CASM algorithm to these frames. In Figure 3, we depict sample results from the proximal, middle, and distal portions of the plaque. Each image is 1.8 cm tall and 2.1 cm wide and the CASM ROI's had a 90% overlap thus providing a smoother image for the 1.2mm by 1.2 mm ROI size. In the mid region, this plaque demonstrated significant shadowing and this is demonstrated by a large calcium classification at the top of the plaque region and thus the bottom half of the plaque is most likely unknown. In the future we will be investigating approaches to handle cases such as this with significant shadowing.

- **What opportunities for training and professional development has the project provided?**

  Nothing to Report

- **How were the results disseminated to communities of interest?**

  Nothing to Report

- **What do you plan to do during the next reporting period to accomplish the goals?**

  *Enrollment:* The primary focus for the next year is to ramp up and maintain enrollment rates in order to meet the goal of full enrollment by month 36. In practice this means that from month 13 to month 36 the CCF site needs to enroll roughly 899 subjects and the VA site needs to enroll 599 subjects. This means an enrollment rate of roughly 9 subjects a week at CCF and 6 subjects a week at VA. (Estimate computed using 50 weeks for the year over two years.) These rates are achievable given the close to 6000 duplex carotid ultrasound exams performed each year at the CCF site and close to 5000 performed at the VA site.

  *Engineering and Scientific Efforts*: While the primary focus is on enrollment, a secondary focus is on manual image segmentation on the collected data. This is critical to enable the work on automated segmentation as well as critical for applying the CASM algorithm to the data. By month 18 we expect to have over 300 cases collected between CCF and VA which will be a reasonable sized data collection to begin development of the convolution neural network based plaque segmentation using the manual borders as the gold standard for training the artificial intelligence based tool.

  In parallel with these efforts, we will be creating the 3D reconstruction software and the associated software code for extracting output from the CASM algorithm in 2D (analyzing specific vessel locations, etc.) and 3D perspectives.

## 4. IMPACT

- **What was the impact on the development of the principal discipline(s) of the project?**

  Nothing to Report

- **What was the impact on other disciplines?**

  Nothing to Report

- **What was the impact on technology transfer?**

  Nothing to Report

- **What was the impact on society beyond science and technology?**

  Nothing to Report

## 5. CHANGES/PROBLEMS:

- **Changes in approach and reasons for change**

  Nothing to Report

- **Actual or anticipated problems or delays and actions or plans to resolve them**

  - **Delay in start of enrollment**

    *Summation*: The difficulty in obtaining safety tested research software for the Sequoia that was capable of collecting the data required for this study led to a 6-7 month delay in starting enrollment. Boosting enrollment is the primary focus for the second year of this grant.

    *Details:* We did not receive the initial research software for the Sequoia ultrasound system until October of 2020 even though the hardware was delivered prior to the start of the grant. Shortly after this installation in October, we realized that the software would require that we send all collected data to Siemens for them to process and send back to us for our analysis. Siemens did not have the support capacity for this type of effort and we could not support the logistics of such an operation where the collected data for each case could easily be greater than 1 GB and the issue of PHI would need extra care in sharing the data with Siemens.
    Siemens recommended that we modify settings on the Sequoia to closely mimic the S3000 system that we had used in the prior study to create the CASM algorithm and

this way avoid the need to send data to Siemens for initial processing. This had the added benefit of producing nearly identical data as the prior study thus insuring compatibility with the CASM algorithm. We agreed to this and obtained the ability to modify the Sequoia on 19 November 2020. By 18 December 2020, we had finalized our quality control testing on the new system settings for the Sequoia. It then took Siemens until 6 April 2021 to build the software release and test it for compliance with FDA safety requirements. In April both the VA and CCF IRB's were updated with the change to the protocol and associated documents and approvals were obtained in June for both the VA and CCF sites. The subsequent HRPO approvals followed at the end of July and mid-August for the VA and CCF sites respectively.

*Plan to Resolve*: The plan is to increase the enrollment rate as described above in section 3, so that we can meet our goal of full enrollment by month 36. This would entail averaging 9 per week for two years at the CCF site and 6 per week at the VA site.

- **510k Application**

  One of the deliverables for this research effort is a 510(k) application. The current research ultrasound system with the position/orientation hardware and software is not a device that is ready for a 510(k) application to the FDA for the following reasons:
  - The research setup is not a production device in either hardware or software
  - The CASM algorithm needs to be integrated onto an already established clinical ultrasound system or there would be an established channel for exporting the raw ultrasound signals from a clinical ultrasound system to a computer where the CASM algorithm resides.

  Effectively, both points require a clinical ultrasound system designed to provide the raw data that is required by the CASM algorithm.

  Our goal remains a 510(k) approval of a medical device containing the CASM algorithm. To achieve this goal, we will continue to engage with Siemens and other ultrasound system manufacturers as potential partners as we obtain results from the efforts described in this report. This research effort and the associated clinical study are critical for obtaining a 510(k) approval.

- **Changes that had a significant impact on expenditures**

  In response to the delay in starting enrollment, we delayed hiring a research coordinator and research technician. These are expected to be hired in quarter 1 of year 2 of this research effort.

  There has also been a delay in finding a replacement for Tanujit Dey (Key personnel, statistician). This individual has been identified and the appropriate paperwork is currently being gathered in order to add them to this research study. We expect them to be added during quarter 1 of year 2.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

  - **Significant changes in use or care of human subjects**

    The ultrasound imaging system used for the research ultrasound exam (Siemens, Sequoia) was modified in a manner that invalidated the FDA 510k approval for the imaging system. Safety testing was performed by Siemens to verify that the modified ultrasound system was within FDA safety requirements for a diagnostic ultrasound system. The IRB's for both sites approved this modification with review by HRPO prior to enrollment of the first subject at either site.

    Protocol Title: "Risk Assessment of Stroke Using Non- Invasive Ultrasonic Backscatter From Carotid Plaque (RUNUP)"
    PI: D. Geoffrey Vince

    Site 1: Cleveland Clinic Foundation, Cleveland, OH
    Site PI: D. Geoffrey Vince
    Annual IRB Review and Approval 10 July 2021
    IRB Study Number 20-602
    HRPO Log Number E01451.1a
    HRPO Approval: 19 Aug 2021

    Site 2: VA Northeast Healthcare System and the Cleveland VA Medical Research & Education Foundation (E01541.1c), Cleveland, OH
    Site PI: Michael Rosenbaum
    VA Northeast Ohio Healthcare System IRB
    Annual IRB Review and Approval 8 Aug 2021
    IRB Study Number 20031-H12
    HRPO Log Numbers E01451.1b and E01451.1c
    HRPO Approval: 30 Jul 2021

  - **Significant changes in use or care of vertebrate animals.**

    Nothing to Report

  - **Significant changes in use of biohazards and/or select agents**

    Nothing to Report

## 6. PRODUCTS

- **Publications, conference papers, and presentations**
  - **Journal publications**

    Nothing to Report
  - **Books or other non-periodical, one-time publications**

    Nothing to Report
  - **Other publications, conference papers, and presentations**

    Nothing to Report
- **Website(s) or other Internet site(s)**

  Nothing to Report
- **Technologies or techniques**

  Nothing to Report
- **Inventions, patent applications, and/or licenses**

  Nothing to Report
- **Other Products**

  Nothing to Report

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

- **What individuals have worked on the project?**

| | |
|---|---|
| Name: | D. Geoffrey Vince |
| Project Role: | Principal Investigator |
| Researcher Identifier (e.g. ORCID ID): | 0000-0001-6155-7118 |
| Nearest person month worked: | 2 |
| Contribution to Project: | Project management including all submissions, manuscripts, and presentations of the research. Oversight and coordination between departments involved in the research effort: Biomedical Engineering, Vascular Medicine, Quantitative Health Sciences, VA, and Siemens. Review, guidance and oversight of data acquisition and data analysis. |
| Funding Support: | NA |

| | |
|---|---|
| Name: | Russell J. Fedewa |
| Project Role: | Co- Investigator at CC site |
| Researcher Identifier (e.g. ORCID ID): | 0000-0002-0690-9472 |
| Nearest person month worked: | 12 |
| Contribution to Project: | Managing regulatory submissions with key sites and collaborators. Development of clinical study protocol and support documents with assistance from co-investigators. Oversight and review of lab personnel for image segmentation. Interim study coordinator role and support for signal and image processing and programming with support for image segmentation and lead for automatic segmentation effort. |
| Funding Support: | NA |

| | |
|---|---|
| Name: | Michael A. Rosenbaum, MD |
| Project Role: | Co-Investigator and Louis Stokes Cleveland VA Medical Center Site PI |
| Researcher Identifier (e.g. ORCID ID): | 0000-0002-1760-9299 |
| Nearest person month worked: | 1 |
| Contribution to Project: | Dr. Rosenbaum is the lead investigator at the Louis Stokes Cleveland VA Medical Center. He has supervised the research team, developed processes for subject enrollment, coordinated activities with the Cleveland Clinic, and reviewed the documents for the IRB and HRPO approval. |
| Funding Support: | No funding support received as Dr. Rosenbaum is a full-time government employee |

| | |
|---|---|
| Name: | Sheronica L. James |
| Project Role: | Research Engineer at CC site |
| Researcher Identifier (e.g. ORCID ID): | 0000-0002-5647-1106 |
| Nearest person month worked: | 12 |
| Contribution to Project: | Lead Scientific programmer for the Borders tool, the CASM algorithm, and the position and orientation data acquisition software. Duties shall also include support of image segmentation efforts. In addition, Ms. James is the research liaison between the VA site and the CCF research team. |
| Funding Support: | NA |

| | |
|---|---|
| Name: | Jaqueline Loftis |
| Project Role: | Research Technician at CC site |
| Researcher Identifier (e.g. ORCID ID): | NA |
| Nearest person month worked: | 12 |
| Contribution to Project: | Lead for manual image segmentation: responsible for performing and training other lab members in image segmentation. Backup data acquisition and recruitment duties and support for technical and regulatory documentation. |
| Funding Support: | NA |

| | |
|---|---|
| Name: | Jerad Williams |
| Project Role: | Research Nurse / Study Coordinator at VA site |
| Researcher Identifier (e.g. ORCID ID): | NA |
| Nearest person month worked: | 9 |
| Contribution to Project: | Mr. Williams has been responsible for the screening, recruitment, and consenting of subjects. He has also assisted with study data collection. |
| Funding Support: | NA |

| | |
|---|---|
| Name: | Manda Double |
| Project Role: | Research Regulatory and Compliance specialist at VA site |
| Researcher Identifier (e.g. ORCID ID): | |
| Nearest person month worked: | 4 |
| Contribution to Project: | Ms. Double has managed the IRB submission and documentation for the Northeast Ohio VA Health System IRB, tracking of human subjects' certification and Conflicts of Interest documentation, and assisted with regulatory audits. |
| Funding Support: | NA |

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

  Name/Role: D. Geoffrey Vince / Principal Investigator
  Description of Change: **Grant Ended Prior to 15 Sep 2020**
  Title: Vascular Plaque Determination for Stroke Risk Assessment
  Sponsor: U.S. Army Medical Research and Material Command, Fort Detrick, Maryland 21702-5012. CDMRP, PRMRP, IIRA W81XWH-16-1-0608

  Name/Role: Russell J. Fedewa / Co-Investigator
  Description of Change: **Grant Ended Prior to 15 Sep 2020**
  Title: Vascular Plaque Determination for Stroke Risk Assessment
  Sponsor: U.S. Army Medical Research and Material Command, Fort Detrick, Maryland 21702-5012. CDMRP, PRMRP, IIRA W81XWH-16-1-0608

- **What other organizations were involved as partners?**

  **Organization Name:** Siemens Medical Solutions USA, Inc.
  **Location of Organization:** 51 Valley Stream Parkway, Malvern PA 19355, USA
  **Partner's contribution to the project:** In-kind support
  Equipment loan: 2 Siemens Sequoia Ultrasound Systems with associated probes, software, service, and engineering support.

  **Organization Name:** Cleveland VA Medical Research and Education Foundation
  **Location of Organization:** 10701 East Blvd, Cleveland, OH 44106-1702, USA
  **Partner's contribution to the project:** Collaboration and Facilities
  Second site for clinical study and scientific collaboration with site personnel.

## 8. SPECIAL REPORTING REQUIREMENTS

Nothing to Report

## 9. APPENDICES

Nothing to Report