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14. ABSTRACT

This report describes the third year of research activities on technologies that support sonographer-supervised robotic systems for breast ultrasound imaging with qualitative elastography, quantitative elastography, and shear-wave elastography. Major objectives achieved in this period include development and evaluation of algorithms for robotically assisted strain elastography that consider uncertainty.

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1. Introduction

The objective of this research project is to develop technologies that support sonographer-supervised robotic systems for breast ultrasound imaging with quantitative elastography. Elastography provides tissue metrics independent of B-mode image features to deliver improved lesion classification, but current techniques are hampered by sensitivity to variations in probe motion and pressure, resulting in significant operator dependence. By delivering advanced, operator-independent elastography data, the proposed system will address the urgent need to improve the positive predictive value (PPV) of ultrasound to spare women unnecessary biopsies, anxiety, and cost while maintaining quality of care. The main goals in the third year of the project have been to develop and experimentally verify novel algorithms for robotically assisted breast ultrasound imaging in preparation for human studies in the final phrase of the period of performance.

2. Keywords

Ultrasound elastography, breast cancer, robotics, human-robot teaming

3. Accomplishments

3.1 What were the major goals of the project

The overall goal of this research is to investigate technologies for improving the positive predictive value (PPV) of ultrasound screening. The specific aims for this research include development and evaluation of a collaborative robotic system for breast ultrasound scanning and elastography (SA1) and perform experiments with robotically assisted elastography in vivo (SA2). Year 1 is focused on developing technologies to support human-robot ultrasound scanning systems, while Years 2-4 transition towards studies and refinement of the collaborative robotic system and ultrasound imaging techniques.

3.2 What was accomplished under these goals

A focus in the third year of performance was on the integration of robot sensor information and uncertainty into quasi-static strain elastography reconstruction. Most state of the art robotically assisted elastography techniques (of which there are few) focus on leveraging robot sensor information for control or occasionally integrate this data into the elastography reconstruction. However, often this is done with a single data sample and typically these approaches fail to account for system uncertainty which can predispose their results to noise. This work utilizes Gaussian filters (a technique common in modern robotic probabilistic mapping approaches) to build a map of tissue elasticity by integrating sensor data and uncertainty into the elastography reconstruction directly. Additionally, it produces a map of model uncertainty, which can be used as a spatially variant measure of confidence in the produced elastogram. Initial experiments to obtain qualitative (relative) elastograms which fused robot joint encoder data were presented at and will be included in the proceedings of the International Symposium on Robotics Research in

October 2019. Data was collected by scanning homemade gelatin phantoms with a 6.5 mm spherical inclusion using the configuration shown in Figure 1.

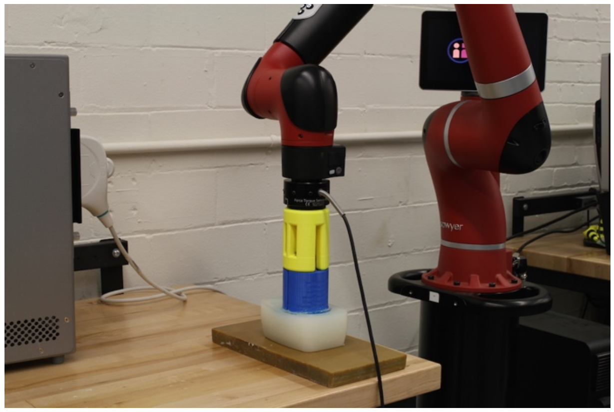

Figure 1. Rethink Robotics Sawyer scanning homemade gelatin inclusion phantom. Force control was performed using a controller derived from the one developed during the second year period of performance. The robot is equipped with a Robotiq Force/Torque sensor (FT 300), a Verasonics ATL L11-4v linear array ultrasound transducer, and a Verasonics Vantage 64LE ultrasound scanning system. Below the phantom is a rubber pad to prevent interference due to echo reflections from the table.

Standard 2D kernel based cross-correlation techniques were used to compute the displacement between pre and post compressed ultrasound RF images. However, the reference (pre-compressed) frame was obtained by taking the median of 5 seconds of data collected at 10Hz, resulting in approximately 50 frames. Then, a small stress was applied to the surface of the phantom and 15 seconds of data was collected (resulting in approximately 150 frames). Displacements were computed between the reference frame and each of the resulting post-compressed samples. Each frame was processed using the proposed probabilistic mapping approach using the FEM mesh as shown in Figure 2. Displacement boundary conditions were computed using the forward kinematics of the robot joint angles and are highlighted in Figure 2. The experiment was repeated for 3 data acquisitions using the same gelatin phantom.

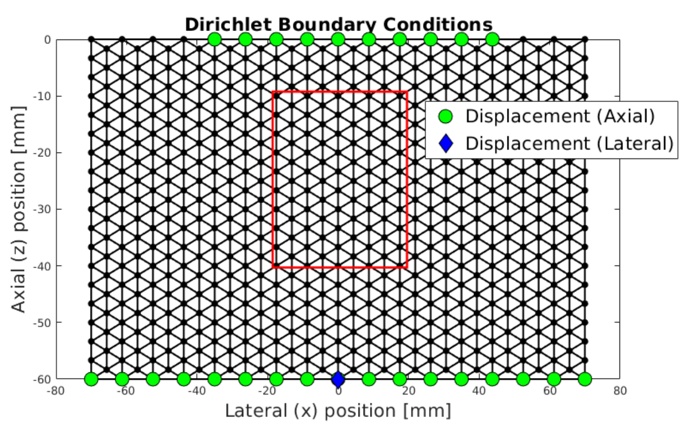

Figure 2. Visualization of the FEM mesh used to perform experiments in the qualitative elastography work. The green circles represent axial boundary conditions due to contact with the transducer or with the table. A single lateral boundary condition was set to zero in the center to prevent sliding during reconstruction. The region visible by the transducer is highlighted by the red rectangle.

Results from the qualitative experiments are shown in Figure 3. The presence of the stiff 6.5 mm spherical inclusion is detectable in the elastograms produced for all three data acquisitions. Moreover, the uncertainty was reduced inside the visible region suggesting improved confidence in the results when compared to the unscanned regions. Results in the third acquisition are less clear, which is believed to be due to out of plane slip induced by the controller.

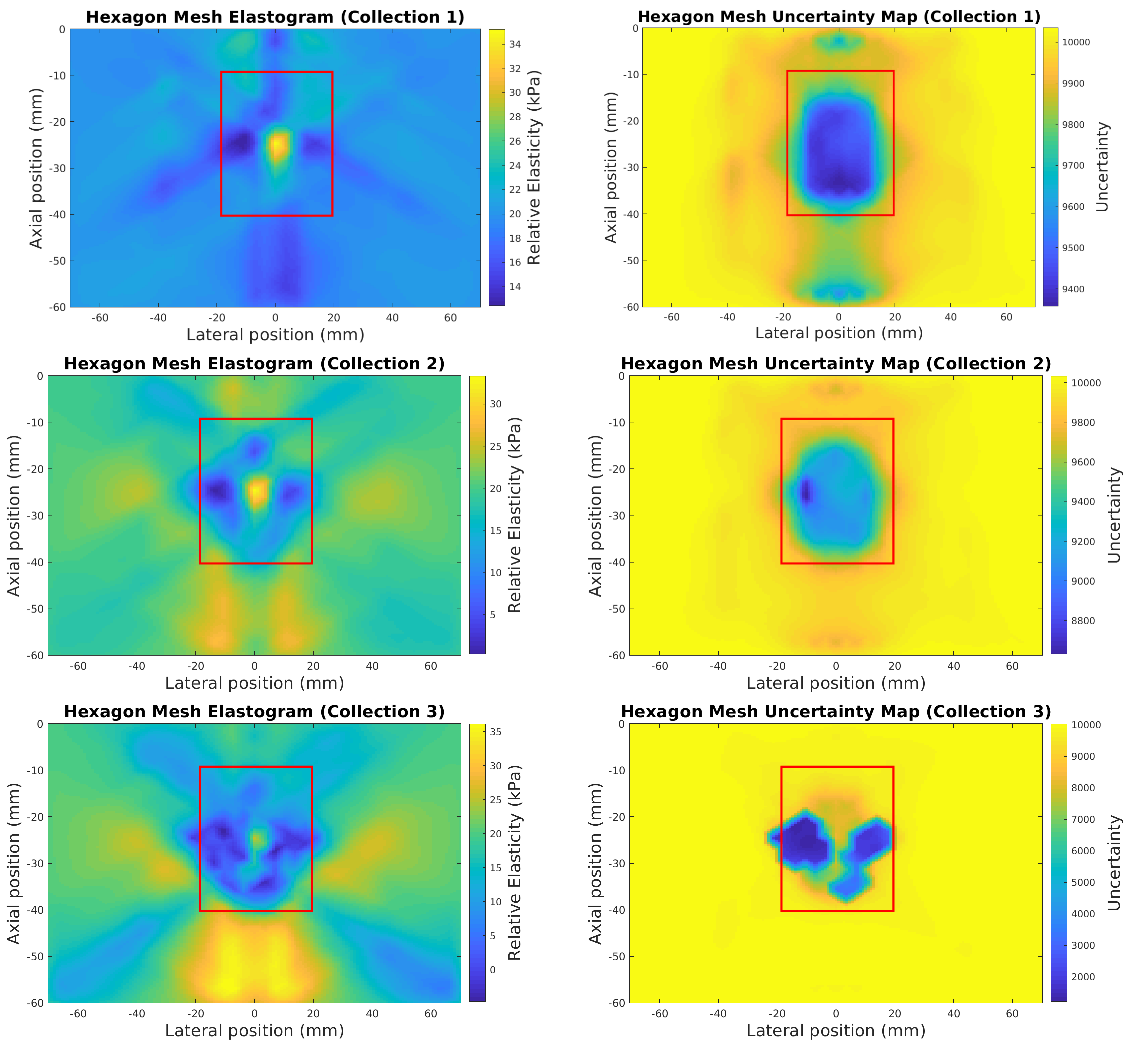

Figure 3. (left) Reconstructed elastograms for all three data acquisitions. (right) Produced uncertainty maps which are produced by fusing measurement uncertainty from displacement calculations as well as uncertainty from joint encoder data and modeling to produce forward kinematics. The region visible to the transducer is highlighted by the red rectangle.

An advantage to using robotic platforms to perform elastography compared to a human sonographer is that additional data can often readily be obtained through integration of additional sensors. One commonly cited disadvantage of strain elastography is that only relative elasticities are produced, therefore qualitative measures of tissue stiffness are available. However, with techniques such as Shear Wave Elastography (SWE), an estimation of the true elastic modulus is produced, which can facilitate quantitative measures. Through integration of a force torque sensor in the proposed probabilistic mapping approach, it is believed that quantitative measures can be obtained for strain elastography. Modifications to the algorithm include force boundary conditions at surface nodes on the FEM mesh which are in contact with the ultrasound transducer as shown in Figure 4.

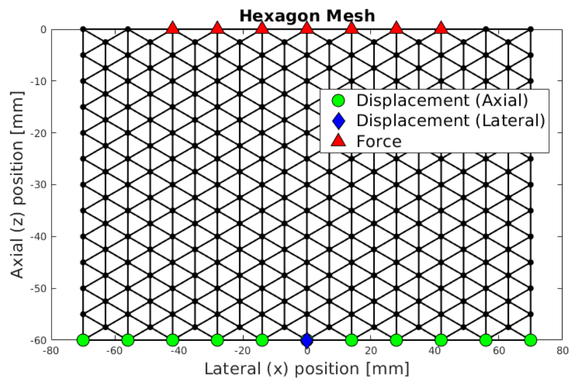

Figure 4. Coarse visualization of an FEM mesh with force boundary conditions illustrated with red triangles. These are nodes which are in contact with the ultrasound transducer. In these experiments, a simplifying assumption was made that the force is applied uniformly across these nodes.

Another modification to the FEM mesh is that a single elasticity term to represent the overall (or average) elastic modulus is included which is shared amongst all nodes. Additionally, the nodes contain terms for changes in elastic modulus just as they did with the qualitative experiments. This term is useful to prevent degrading results due to poor initialization of the average elasticity (for example, if the background elasticity was 15kPa but the algorithm was initialized with 50kPa). An elastogram was reconstructed using the data obtained from the qualitative experiments (measured wrenches were previously stored as well) and the result is shown in Figure 5.

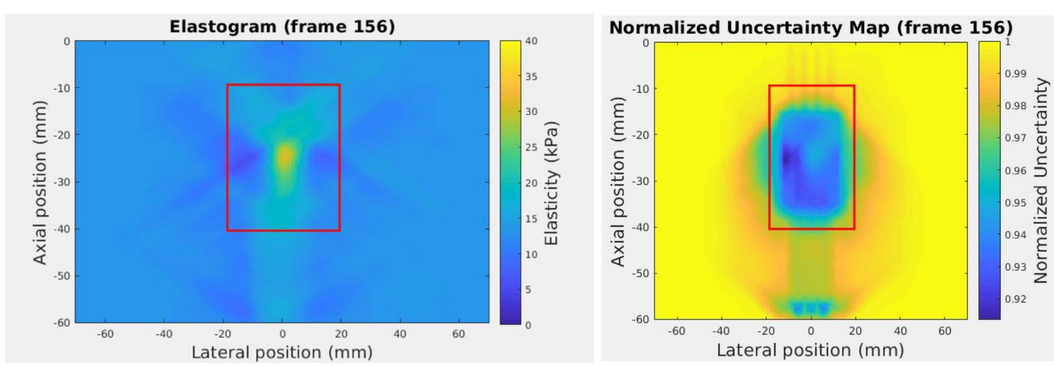

Figure 5. Reconstructed quantitative elastogram (left) and produced uncertainty map (right). The 6.5mm inclusion is visible in the elastogram and the background elasticity is approximately 18kPa which was verified using SWE. As with the qualitative experiments, uncertainty in the visible region (highlighted by the red triangle) was reduced as a result of the probabilistic reconstruction process.

Another benefit of robotic assistance is that the system does not fatigue in the same way that a human sonographer might. Therefore, full tissue scans are feasible whereas they would have been very difficult for a human to perform repeatedly. To facilitate this type of scanning, the controller was modified to include position and orientation of the transducer in addition to a force observer and axial force control. An example of full tissue scanning using this controller is shown in Figure 6.

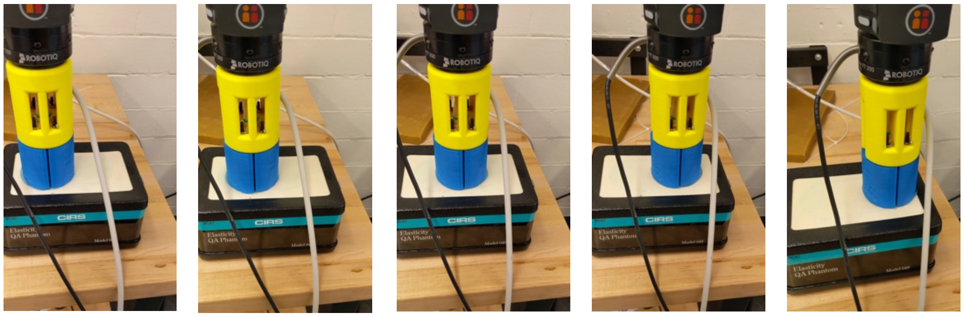

Figure 6: Time lapse of controller performing scanning motion on a CIRS inclusion phantom using the new position, force, and orientation controller. This modification will facilitate full tissue scanning and reconstruction using the probabilistic tissue mapping approach.

A wide homemade gelatin phantom with a 6.5 mm inclusion was scanned using the procedure illustrated in Figure 7. Data from the force torque sensor and joint encoders was collected and stored for offline processing. Additionally, the same procedure as used in the qualitative experiments to obtain reference and post-compressed frames was performed during the scanning in different locations. One modification was made which extended the duration of data collection during the post compressed phase from 15 seconds to 30 seconds to roughly double the amount of data for analysis. The data is currently in the process of being analyzed, and based on what is learned from this experiment, future experiments may be similar.

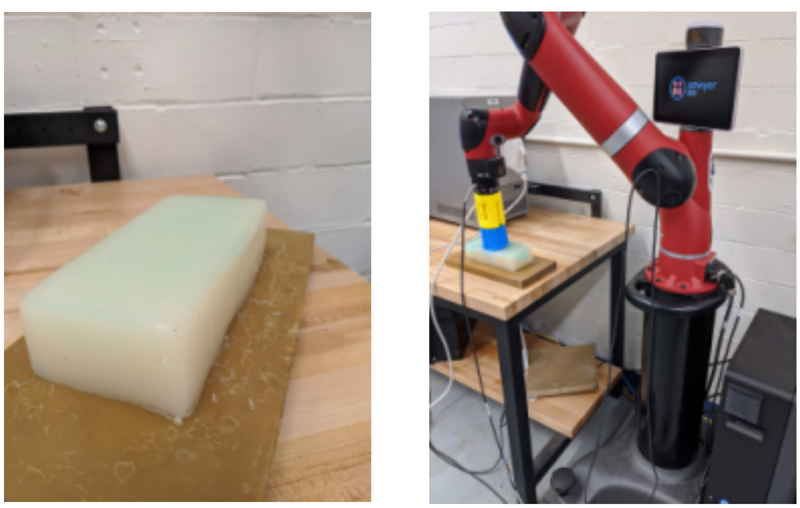

Figure 7: Homemade wide gelatin inclusion phantom (left) and scanning procedure (right). The data collected from this experiment will be used to inform future quantitative elastography reconstruction experiments. Leveraging the modifications made to the controller facilitate this scanning procedure which could potentially be used to perform full tissue scans and reconstructions.

In this project period we also have continued development of *non-linear* elasticity imaging methods, with the goal of improving discrimination of benign and malignant lesions. In the previous project period (2018-2019) we developed and implemented an algorithm based on combined 2D strain imaging and shear wave elastography. This method, reported in *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, provides quantitative 2D images of non-linear shear modulus. As described, the method was limited to axial strains.

In this period, we have improved upon this work by developing a method that models complex strain fields due to both axial and lateral motions of the imaging transducer. This approach, termed "Shear Induced Nonlinear Elasticity (SiNe) imaging, produces correct images of non-linear shear modulus, whether the applied strain is axial, lateral, or a combination of the two. The Sine method is described below (Figure 8).

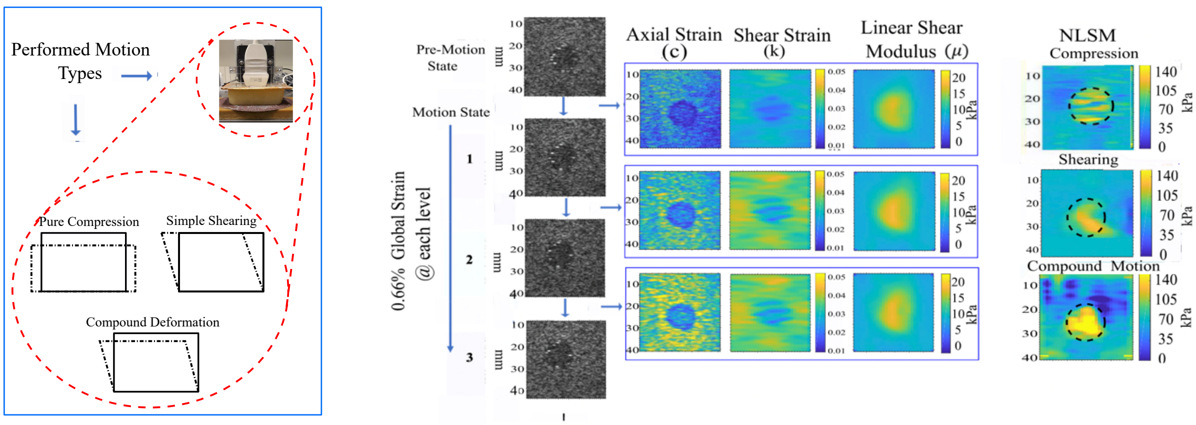

Figure 8. Depiction of SiNe imaging process. At left (blue box) is a schematic representation of the modes of tissue deformation that may be applied to generate the non-linear shear modulus estimate (NLSM). At center, a sequence of B-mode images obtained during compound deformation of the tissue. 2D tracking of inter-frame motion provides maps of axial (c) and shear (k) strain. Shear wave elastography is used to generate matched maps of apparent linear shear modulus μ. At far right are maps of non-linear shear modulus obtained using estimators designed for axial motion alone (top, "compression") lateral motion alone (center, "shear") and combined motions (bottom, "compound"). The newly developed compound estimator produces the most accurate reconstruction of the inclusion.

We expect that it will not be possible to apply purely axial deformation of breast tissue with freehand scanning in practice. We have therefore developed the SiNe approach, which allows complex, compound motions to be tracked. The SiNe model extracts axial and lateral strain data concurrently with shear-wave elastography derived estimates of shear modulus to produce a map of non-linear shear modulus. A further advantage of this approach is that we have found reliable estimates of non-linear shear modulus can be made with smaller strains by using a shear deformation, rather than axial compression, as shown in Figure 9.

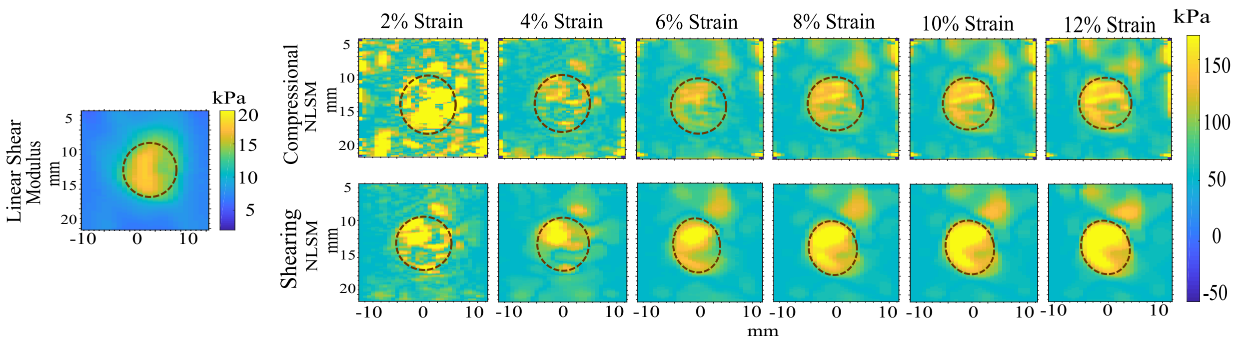

Figure 9: NLSM maps estimated in tissue-mimicking phantoms by pure compression and simple shearing for an 18 kPa inclusion in 8 kPa gelatin medium for different strain levels. The dotted circle shows the original inclusion position. Note that the NLSM map converges at ~4% strain in the shear case (bottom), while axial compression (top) requires approximately twice the strain to converge to the final estimate.

We have obtained excellent agreement between finite-element simulations of the SiNe image approach and results obtained in tissue-mimicking phantoms, as shown in Figure 10. We are prepared to perform measurements in excised tissue samples embedded in gel in anticipation of in-vivo studies.

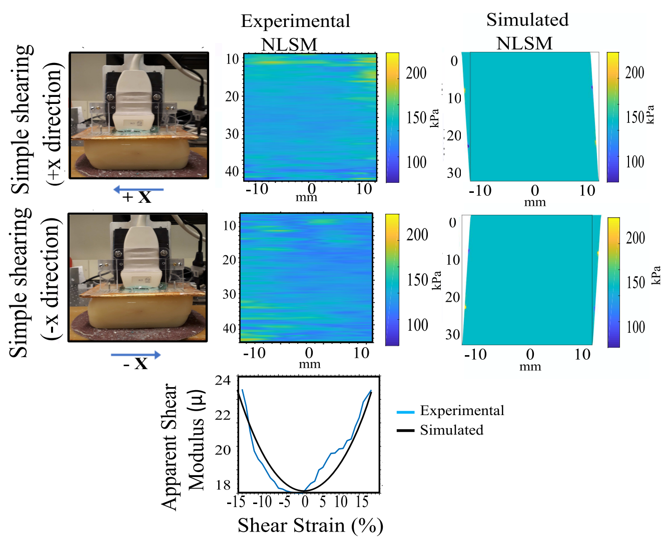

Figure 10: Representative results for shearing experiments, top row for lateral shearing on +direction and bottom row for -x direction on the phantom. Both lateral shearing directions give similar estimates of NLSM and the apparent shear modulus.

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

This project has been a part of professional development for two graduate students in PI Howard's Robotics and Artificial Intelligence Laboratory. The research on hybrid force/velocity control for acquiring ultrasound scans under constant force and position setpoints supported the work of Christian Freitas as described in the 2017-2018 annual report in preparation of his master's thesis in Electrical Engineering that he defended in April 2018. The work on stiffness estimation from strain elastography for adaptive hybrid force/velocity control is one of the principal research topics of Michael Napoli's doctoral research. Michael is actively preparing his PhD Thesis proposal on the topic of quantative robotically assisted elastography. Both of these individuals have published peer-reviewed research on topics supported by this grant.

This project has also supported one undergraduate and one graduate student in PI McAleavey's ultrasound imaging laboratory. Undergraduate Katelyn Offerdahl (2017-2018) worked to quantify the performance of shear wave elasticity imaging methods during periods of transducer motion. Her work led to a conference publication in the first year of this project. The work on co-registered shear strain and shear wave speed imaging is the thesis topic of graduate student Soumya Goswami, who continues to be supported by this grant.

3.4 How were the results disseminated to communities of interest?

Results were disseminated to communities of interest through publication of refereed conference papers and research presentations at academic conferences as outlined in Section 6.1.

3.5 What do you plan to do during the next reporting period to accomplish these goals?

During the next reporting period (2/2020-1/2021) we plan to prepare and perform in vivo experiments of our platform for research in robotically assisted medical ultrasound. This will include working with Dr. O'Connell to train sonographers and develop a suitable scanning procedure. We will also continue technology development as described in the engineering research activities described in RT1-ST4.

4. Impact

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

Nothing to report for this period beyond the publications and presentations listed below.

4.2 What was the impact on other disciplines?

Nothing to report for this period.

4.3 What was the impact on technology transfer?

There was no technology transfer that occurred under this project during the 2018-2019 period of performance.

4.4 What was the impact on society beyond science and technology?

Nothing to report for this period.

5. Challenges / Problems

5.1 Changes in approach and reasons for change

As described in last year's report we continue to use human positioning as the principal mode of placing the transducer in contact with phantoms. In parallel to the development and testing of the control and estimation algorithms on our Rethink Robotics Sawyer Collaborative Robot and in response to the manufacturer of that robot closing in Fall 2018, PI Howard acquired a KUKA LBR Med robot with non-project funds to transition the developed technology onto during the next year of the period of performance. This robot is a better analog for a robotic system that could be integrated in future medical applications. We are also preparing an update to our IRB protocol based on the feedback of Dr. O'Connell that will be submitted for approval before the start of human subject studies involving the robotic manipulator. Human studies will not begin before these protocol changes have been approved.

5.2 Actual or anticipated problems or delays and actions or plans to resolve them

There are no problems or significant delays to report. With respect to sonographer training for use of the robotic system, we are delayed with respect to the revised statement of work. We anticipate starting sonographer training once the IRB protocol changes that we plan to request are approved.

5.3 Changes that had a significant impact on expenditures

The no-cost extension and increase in student support costs have impacted the budget with respect to graduate student support.

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

There were no significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents.

6. Products

6.1 Publications, conference papers, and presentations

Papers and a PhD thesis proposal on the stiffness and uncertainty estimation using the robotically assisted ultrasound platform are in preparation at this time. Papers published during this year's period of performance are listed below.

Publications:

1) M. Napoli, S. Goswami, S. McAleavey, M. Doyley, and T.M. Howard, "Probabilistic Mapping of Tissue Elasticity for Robot-Assisted Medical Ultrasound," In International Symposium on Robotics Research, October 2019.
2) S Goswami, R Ahmed, M Doyley, S McAleavey, “Nonlinear Shear Modulus Estimation with Bi-axial Motion Registered Local Strain*”, IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control* 66(8), pp. 1292-1303, May 2019
3) S. Goswami, S. Khan, R. Ahmed, M. M. Doyley and S. A. McAleavey, "Deformation Independent Non-linearity Estimation: Studies and Implementation in Ultrasound Shear Wave Elastography," *Proceedings of the 2019 IEEE International Ultrasonics Symposium (IUS)*, Glasgow, United Kingdom, 2019, pp. 217-220.
4) S. Goswami, R. Ahmed, S. Khan, MM. Doyley, SA. McAleavey, “Shear Induced Non-linear Elasticity Imaging (SiNe): Elastography for Compound Deformations”, IEEE Transactions on Medical Imaging (submitted)

Theses: N/A

Presentations:

1) M. Napoli, S. Goswami, S. McAleavey, M. Doyley, and T.M. Howard, "Probabilistic Mapping of Tissue Elasticity for Robot-Assisted Medical Ultrasound," Presented at the International Symposium on Robotics Research, Hanoi, Vietnam, October, 2019.
2) S. Goswami, R. Ahmed, M. M. Doyley, S. A. McAleavey, ““2D tracking improves quantitative nonlinear shear modulus estimation,” Presented at the International Symposium on Ultrasonic Imaging and Tissue Characterization, Arlington, VA, June, 2019
3) S. Goswami, S. Khan, R. Ahmed, M. M. Doyley and S. A. McAleavey, "Deformation Independent Non-linearity Estimation: Studies and Implementation in Ultrasound Shear Wave Elastography," Presented at the 2019 IEEE International Ultrasonics Symposium (IUS), Glasgow, United Kingdom, October 2019
4) S. Goswami, S. Khan, R. Ahmed, M. M. Doyley and S. A. McAleavey, "Deformation Independent Non-linearity Estimation,” Presented at the Rochester Center for Biomedical Ultrasound Symposium, Rochester, NY, November 2019

6.2 Website(s) or other Internet site(s)

There are no websites or internet sites to report.

6.3 Technologies or techniques

There are no technologies or techniques to report.

6.4 Inventions, patent applications, and/or licenses

There are no inventions, patent applications, and/or licenses to report.

6.5 Other products

There are no other products to report.

7 Participants & other collaborating organizations

7.1 What individuals have worked on the project?

Name:	*Stephen McAleavey*
Project Role:	*PI*
Researcher Identifier:	*eRA Commons User ID: smcaleavey*
Nearest month worked	*2*
Contribution to Project:	*Human subjects protocol development and approval, ultrasound shearwave elastography systems development*
Other Funding Support:	*NIH, NYSTAR*

Name:	*Thomas Howard*
Project Role:	*PI*
Researcher Identifier:	*IEEE PIN: 107736*
Nearest month worked	*1*
Contribution to Project:	*Design and development of software robotically assisted breast ultrasound scanning system, design and development of hybrid force/velocity control, simulation and haptic interface software, assisted with development of qualitative and quantitative elastography algorithms.*
Other Funding Support:	*NSF, ARL, NASA*

Name:	*Marvin Doyley*
Project Role:	*Co-PI*
Researcher Identifier:	*eRA Commons User ID: mmdoyley*
Nearest month worked	*1*

Contribution to Project:	*Strain elastography system development lead*
Other Funding Support:	*NIH*

Name:	*Michael Napoli*
Project Role:	*Graduate student*
Researcher Identifier:	*IEEE PIN: 198132*
Nearest month worked	*12*
Contribution to Project:	*Development of controllers and estimators for robotically assisted breast ultrasound scanning system, experiments on hybrid force/velocity controller software capabilities for strain elastography, integration of the elastography software stack with arm control software, interfaces, and sensors, development of new qualitative and quantitative elastography algorithms.*
Other Funding Support:	*N/A*

Name:	*Soumya Goswami*
Project Role:	*Graduate student*
Researcher Identifier:	--
Nearest month worked	*8*
Contribution to Project:	*Shear wave and strain elastography sequence development, Phantom validation studies*
Other Funding Support:	*University of Rochester Department of Electrical Engineering*

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

PI Howard was awarded the NASA Early Career Faculty Award in October 2019 on a project that will overlap with the final year of the period of performance of this grant.

7.3 What other organizations were involved as partners?

There are no other organizations involved as partners in this research.

8 Special reporting requirements

There are no special reporting requirements. This report reflects the work of PI McAleavey under Award Number W81XWH-17-1-0021 and PI Howard under Award Number W81XWH-17-1-0022. Leadership and organization of research tasks have been marked with the responsible PI and site of the research activities.