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TITLE: Assistive and Autonomous Breast Ultrasound Screening: Improving PPV and Reducing RSI

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14. ABSTRACT

This report describes the second year of research activity on technologies that support sonographer-supervised robotic systems for breast ultrasound imaging with quantitative elastography and shear-wave elastography. Major objectives achieved in this period include controller and estimator development and experimental validation of robotically assisted strain elastography. Ultrasound pulse sequence development and verification continued in this period, with the development and test of non-linear shear modulus imaging codes and phantom validation.

15. SUBJECT TERMS

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Table of Contents

Page

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 second year of the project have been to develop and experimentally verify the algorithms for robotically assisted breast ultrasound imaging in preparation for human studies in the third year 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 implementation of a robotic arm control system with haptic interface 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 Year 2 and Year 3 will transition towards studies and refinement of the control system and haptic interface.

3.2 What was accomplished under these goals

The research tasks involving development of technologies for robotic ultrasound scanning hardware, software, and systems (RT1) were led by PI Thomas Howard of the Robotics and Artificial Intelligence Laboratory at the University of Rochester. Tasks involving development of elasticity software and ultrasound imaging (RT2), imaging subjects pre-biopsy (RT3), and analysis of in vivo data (RT4) were led by PI Stephen McAleavey in the Department of Biomedical Engineering at the University of Rochester.

Subtasks involving robotic ultrasound scanning hardware, software, and systems (RT1) include final arm and haptic interface selection, ultrasound transducer/robot end-effector design and machining (RT1-ST1, McAleavey/Howard), implementation and testing of arm/haptic interface control system (RT1-ST2, Howard), and validation of inverse kinematic model and force measurement, constant pressure/constant position mode validation, and human safety verification (RT1-ST3, Howard). The milestone for RT1 included the design goals achieved with quantification of arm mechanical properties (RT1-M1, McAleavey/Howard). The statement of work was also recently updated to detail tasks for robotic software development concerning learning-based algorithms for guiding scan locations and mechanisms for bi-directional communication (RT1-ST4), which will involve improvements for how the robot will estimate the state of and plan interactions with scanned tissue. As detailed in the 2017-2018 annual report, we developed a system for robotically assisted ultrasound scanning composed of a compliant robotic manipulator, a force/torque sensor, a wrist-mounted ultrasound transducer, a haptic interface device, and a ultrasound scanning device under RT1-ST1 and developed and experimentally quantified the performance of a hybrid force/velocity controller for robotically-assisted strain elastography under subtasks RT1-ST2 and RT1-ST3, which satisfied milestone RT1-M1. During this second year of the period of performance we continued to improve on the hardware, software, interface, and control algorithms in several ways that will be discussed in the context of the elastography software development (RT2) subtasks that were the focus of this year's activities.

Subtasks of RT2 include phantom design (RT2-ST1, McAleavey/Doyley), implementation of combined shear wave and strain elastography for viscoelastic, poroelastic, and non-linear modulus imaging (RT2-ST2, McAleavey/Doyley), phantom validation of elastography software using laboratory systems (RT2-ST3, McAleavey/Doyley), and phantom validation of elastography software using robotic arm system (RT2-ST4, Howard/McAleavey/Doyley). The milestones for RT2 are in vitro validation of robotic arm elastography system (RT2-M1, Howard/McAleavey/Doyley) and publish a paper on implementation of robotically assisted elastography (RT2-M2, Howard/McAleavey/Doyley). Activities described in the 2017-2018 annual report describe efforts to satisfy RT2-ST1 and RT2-ST2. During the second year of the project we developed many gelatin and cryogel phantoms and utilized the commercial ultrasound breast anatomical phantoms under RT2-ST1 and utilized the shear wave and strain elastography imaging sequences on the Verasonics 64 LE system under RT2-ST2 to assist with quantifying the performance of the robotically assisted breast ultrasound system.

Under RT2-ST2 and ST3 we have developed elastography imaging sequences on the Verasonics 64 LE system and demonstrated the ability to image linear and non-linear shear modulus in phantoms. We have been able to show good correspondence between values obtained using ultrasound elastography and those achieved through unconfined mechanical compression, as illustrated in Figure 1.

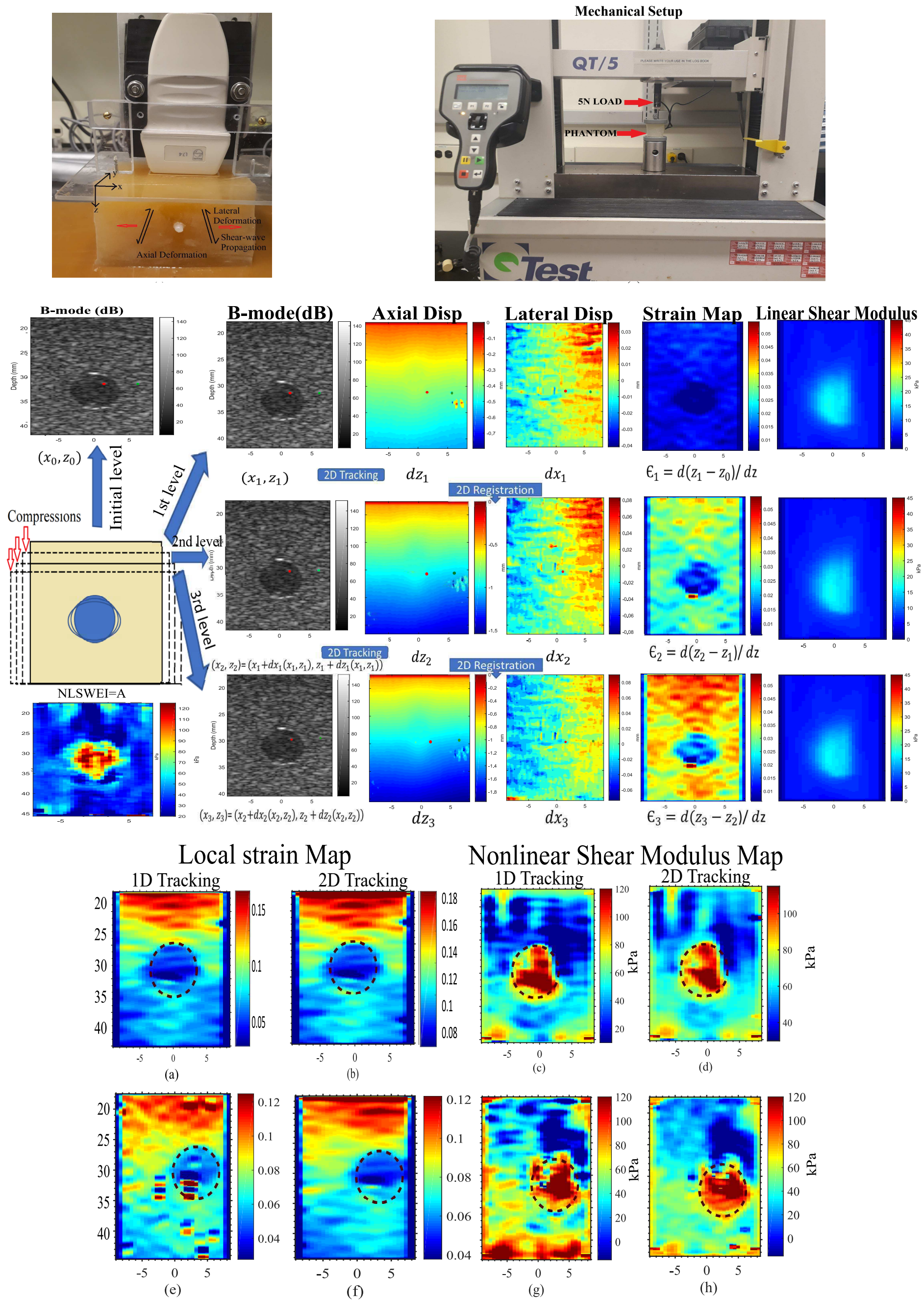

Figure 1. (top left) Experimental setup for imaging strain and shear wave speed in phantom with Verasonics 64LE system. (top right) System for unconfined compression measurement of phantom mechanical properties for validation of ultrasound elastography results. (center) Illustration of the non-linear strain imaging process developed. Progressive compression of the phantom is tracked using data from multiple plane-wave B-mode imaging sequences to produce maps of axial and lateral displacement. These maps allow registration of shear wave speed images (not shown) compensate for large-strain motion of the phantom. Linear shear modulus images are extracted from shear wave speed data, while non-linear modulus images (NLSWEI) image results from the dependence of shear wave speed on local strain. (bottom) Comparison of linear strain and nonlinear shear modulus maps illustrating improved image quality with 2D strain tracking.

Under RT2-ST3, we have demonstrated that the 2D motion tracking techniques we have developed for this project yield improved non-linear shear wave speed images compared to uniaxial tracking methods disclosed previously. With respect to RT2-M1, we have submitted for publication a paper on combined strain and shear wave speed imaging.

Another major focus of our work during the second year of the period of performance involved phantom validation of integrated strain and shear-wave elastography using robotic arm positioning under RT2-ST3. Part of this work resulted in the satisfaction of milestone RT2-M2 by publishing a paper titled “Hybrid Force/Velocity Control with Compliance Estimation via Strain Elastography for Robot Assisted Ultrasound Screening” that was accepted to and presented at 7th IEEE International Conference on Biomedical Robotics and Biomechatronics (BioRob) in August 2018 by ECE PhD Student Michael Napoli. This research built upon work in support of Christian Freitas’s MS Thesis in Electrical Engineering, which he defended in April 2018. The BioRob 2018 paper studies the performance of the hybrid force/velocity controller on a 25 kPa tissue phantom starting with initial elasticity estimates in the range of 15 kPa to 85 kPa. The experiments studied the transient response to a force step input along the main axis of the transducer with and without elastography-based feedback (Figure 2). Experimental results demonstrate the utility of using the elastography-based feedback for improving the model inside of the hybrid force/velocity controller for improving the transient response of the feedback controller.

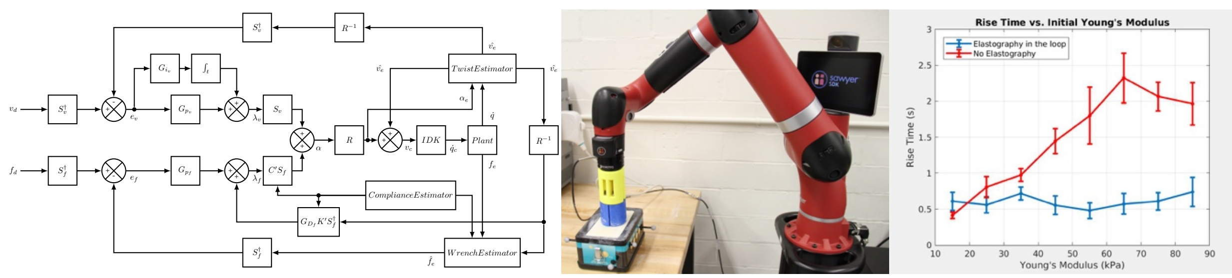

Figure 2. (left) Hybrid force/velocity control algorithm for controlling the position and pressure of the ultrasound transducer with a tissue phantom. (center) The experimental setup of the hybrid force/velocity control experiments. (right) Quantitative results showing improved transient response performance using elastography feedback inside of the control loop.

A second outcome from these experiments showed how we can improve the convergence properties for the elastography optimization routine by modifying the regularization to penalize solutions that significantly deviate from the previous step. Figure 3 illustrates the convergence behavior of the original and updated optimization routines for from different initial conditions.

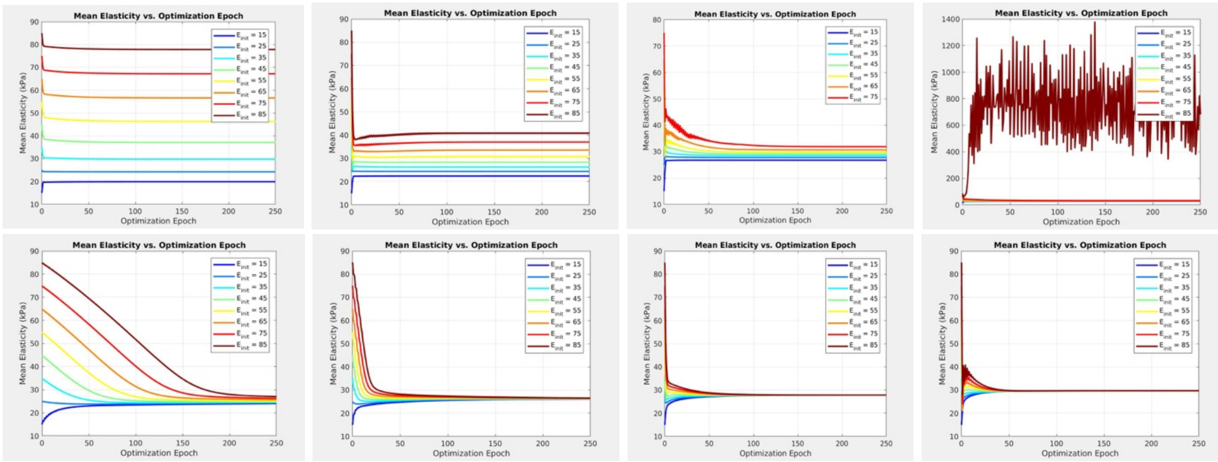

Figure 3. (top row, left to right) Tikhonov Regularization assuming alpha from 10^{-11} (top left) to 10^{-14} (top right). (bottom row, left to right) Modified Tikhonov Regularization assuming alpha from 10^{-11} (bottom left) to 10^{-14} (bottom right). The Modified Tikhonov Regularization algorithm demonstrated better converge properties over a wide range of initial stiffness estimates.

One observation of the elastography-in-the-loop control experiments from the BioRob 2018 paper was that the optimally tuned controller parameters varied over different phantom stiffness values. To further improve the controller performance, we studied tuned controller parameters over a wide range of phantom stiffnesses to develop a stiffness-dependent controller gain scheduler. Figure 4 illustrates how we calculated the rise time and overshoot of the transient response while Figure 5 shows the mean overshoot and mean rise time of the hybrid force/velocity controller under constant and adaptive gain parameters. On average, the stiffness-based gain scheduler achieved near the desired step response for all phantoms in the study.

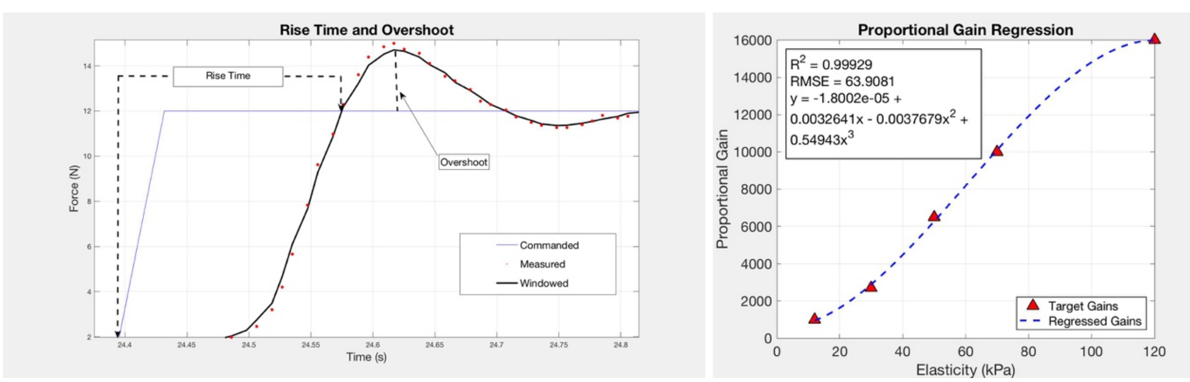

Figure 4. (left) Illustration of the rise time and overshoot calculations on the transient response of the controller when subject to a step input of force. (right) A chart illustrating the tuned proportional gains as a function of the tissue stiffness.

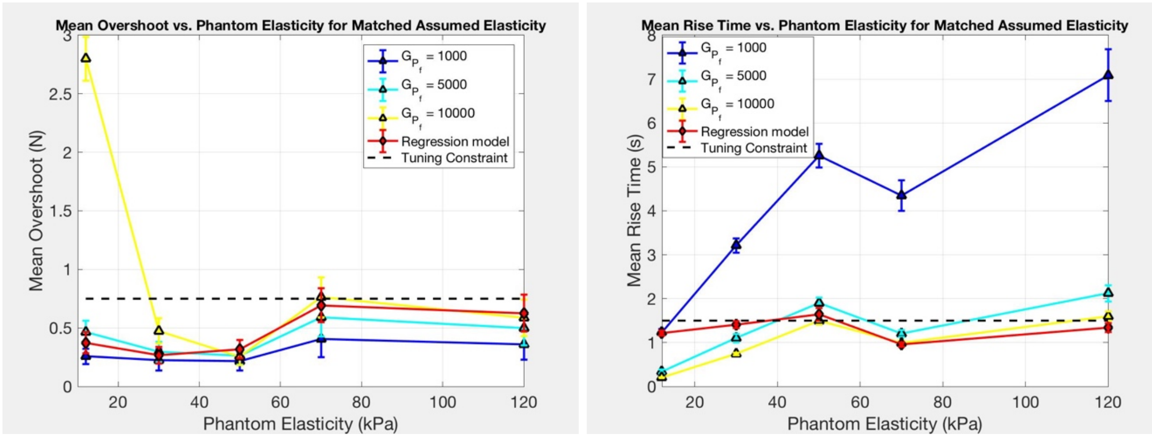

Figure 5. (left) The mean overshoot as a function of controller gain parameters. (right) The mean rise time as a function of the controller gain parameters.

During this year's period of performance, we also made progress with integration of shear-wave elastography in the robotically assisted ultrasound scanning system. We developed a new mount for the transducer used in the shear wave experiments using the hybrid force/velocity controller and studied the signal-to-noise (SNR) of control with various stiffness assumptions against a baseline of a static transducer held by a fixed transducer mount. As expected, Figure 7 shows that the SNR of the fixed mount outperformed the SNR obtained by the hybrid force/velocity controller but provided an estimate of relative performance.

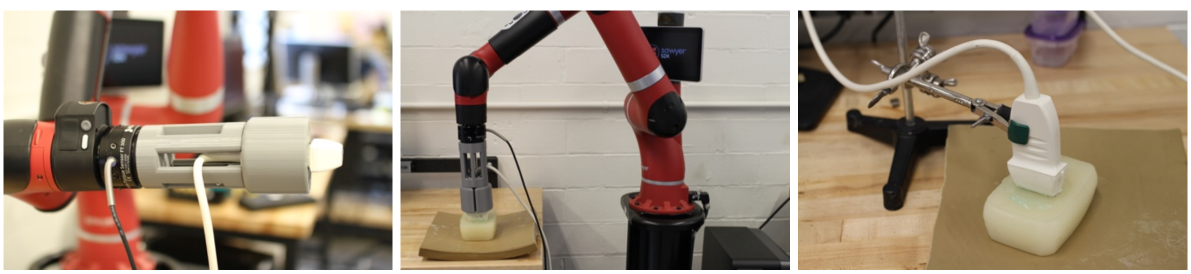

Figure 6. (left and middle) Images showing a new transducer mount for shear wave elastography experiments. (right) Fixed transducer mount for comparative baseline of shear wave elastography experiments.

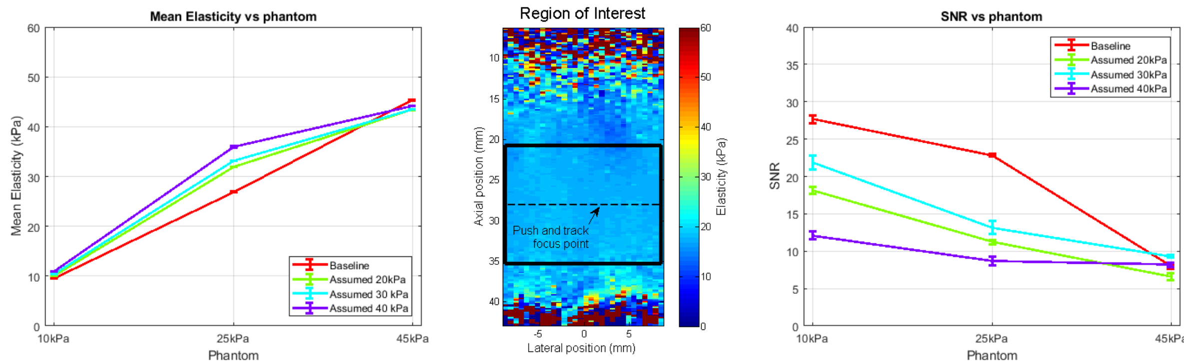

Figure 7. (left) Mean estimated elasticity of a phantom observed using shear wave elastography as a function of actual phantom stiffness, (middle) Illustration of window used for SNR calculation of shear wave elastography, (right) SNR as a function of actual phantom stiffness.

Lastly, we have begun to formulate a variation of the quasi-static strain elastography algorithm that incorporates observations provided by multiple measurements and provide a more accurate model of uncertainty in the estimated elastogram. This procedure, which is grounded in the mathematics of simultaneous localization and mapping, aims to estimate and compensate for transducer displacements when making observations. Research into these approaches are ongoing and will provide an important foundation for research in learning-based approaches to guiding scan locations in RT1-ST4 during the third year of the period of performance.

The research tasks involving SA2 include imaging of subject's pre-biopsy (RT3) and analysis of in vivo data (RT4). Subtasks of RT3 include submitting documents for IRB review (RT3-ST1, McAleavey), train sonographers and students in scanning procedure (RT3-ST2, McAleavey/Howard/O'Connell), recruiting 72 patients for imaging (RT3-ST3, McAleavey/O'Connell), and scanning patients (RT3-ST4, McAleavey/O'Connell). Milestones of RT3 include IRB approval received (RT3-M1, McAleavey) and 72 patients scanned (RT3-M2, McAleavey). Subtasks of RT4 include collecting histology data (RT4-ST1, McAleavey/O'Connell) and statistical analysis of poroelastic, viscoelastic, and non-linear parameters vs histology and BiRADS category (RT4-ST2, McAleavey). The only milestone of RT4 is to publish the results of in vivo measurements and statistical analysis (RT4-M1, McAleavey/Doyley/Howard/O'Connell).

With respect to RT3, we have accomplished ST1 and M1: receiving approval (and renewal) of IRB approval for this study. Training of sonographers in the use of the robotic system will begin in the next project period in consultation with co-investigator Dr. O'Connell.

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. Both of these individuals have published peer-reviewed research on the topic supported by this grant.

This project has supported one undergraduate and one graduate student in PI McAleavey’s ultrasound imaging laboratory. Undergraduate Katelyn Offerdahl worked to quantify the performance of shear wave elasticity imaging methods during periods of transducer motion. Her work led to a conference publication. The work on co-registered shear strain and shear wave speed imaging is the thesis topic of graduate student Soumya Goswami, 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 (2/2019-1/2020) we plan to prepare and begin 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 new 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

On the robotic technology development research tasks, we expanded our efforts to simulate the response of the robot controller in response to risks imposed by the manufacturer of the robotic manipulator used in this project closing in Fall 2018. We also still continue to use human positioning as the principal mode of placing the transducer in contact with phantoms based on the ease of this mode of interaction however, we still intend to continue integrating the haptic interface control software that we developed and reported on during this year's period of performance as a second mode of robotically assisted breast ultrasound scanning system control.

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 slightly delayed with respect to the approved statement of work. We anticipate starting this training in the next project period.

5.3 Changes that had a significant impact on expenditures

We have spent less than anticipated on graduate student support in part because of delays in graduate student recruiting due to fixed admissions schedules and graduate students supported by multiple research projects.

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, articles, and theses on the adaptive stiffness estimation for control of the robotically-assisted ultrasound platform are in preparation for submission to academic conferences at this time. Papers published, theses defended, and presentations given during this year's period of performance are listed below.

Publications:

1) M. Napoli, C. Freitas, S. Goswami, S. McAleavey, M. Doyley, and T.M. Howard, "Hybrid Force/Velocity Control with Compliance Estimation via Strain Elastography for Robot

Assisted Ultrasound Screening," In 7th IEEE International Conference on Biomedical Robotics and Biomechatronics. IEEE, Aug. 2018.
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 (submitted)

Theses:
1) C.Freitas, "Hybrid force/velocity control for semi-autonomous ultrasound scanning," Master's thesis, University of Rochester, Apr. 2018.

Presentations:
1) M. Napoli, C. Freitas, S. Goswami, S. McAleavey, M. Doyley, and T.M. Howard, "Hybrid Force Velocity Control with Compliance Estimation via Strain Elastography for Robot Assisted Ultrasound Scanning", presented at the Inaugural RCBU Biomedical Ultrasound Symposium Day, Rochester, NY, USA. Nov. 2018.
2) S. Goswami, R. Ahmed, M. Doyley, S. McAleavey, "Nonlinear Shear Modulus Estimation with Biaxial Motion Registered Local Strain Distribution", presented at the Inaugural RCBU Biomedical Ultrasound Symposium Day, Rochester, NY, USA. Nov. 2018.

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	*2*
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,*
Other Funding Support:	*NSF, ARL*

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	*6*
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.*
Other Funding Support:	*NSF*

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*

Name:	*Katelyn Offerdahl*
Project Role:	*Undergraduate student*
Researcher Identifier:	--
Nearest month worked	*1*
Contribution to Project:	*Quantification of ultrasound beam sequence parameters on signal-to-noise and contrast-to-noise ratios of shear wave elastograms. Quantification of elastogram noise due to probe or tissue motion. Development of test fixtures*
Other Funding Support:	

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 has continued his yearly subtasks under the Army Research Laboratory Robotics Collaborative Technology Alliance subtask with a period of performance that continues through Fall 2019.

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.