UITC ABSTRACTS 2019

Wednesday morning

1. TISSUE PARAMETERS 1

1.1 **Breast lesion characterization using quantitative ultrasound mean-values, texture, and texture-derivates**, Laurentius Osapoetra, Lakshamanan Sannachi, Hadi Moghadas, Daniel DiCenzo, Karina Quiaoit, Kashuf Fatima, Gregory Czarnota, *Department of Radiation Oncology, and Physical Sciences, Sunnybrook Health Sciences Centre, Sunnybrook Research Institute, Toronto ON, Canada, gregory.czarnota@gmail.com*

Objectives: Previous studies have demonstrated the efficacy of QUS parametric maps in conjunction with textural features for non-invasive characterization of breast lesions. In this study, we expand the QUS feature space through the addition of texture-derivates and perform breast lesions characterization in a larger cohort of patients.

Methods: Radiofrequency (RF) breast ultrasound data were acquired from 193 patients (101 benign and 92 malignant) with suspicious breast lesions using clinical ultrasound imaging system, operating at a 6 MHz transmit frequency. QUS Spectral parameters including mid-band fit (MBF), spectral slope (SS), and spectral intercept (SI) and backscatter coefficient parameters including average scattering diameter (ASD) and average acoustic concentration (AAC) were calculated from the tumor. Subsequently, texture analysis using gray-level co-occurrence matrices (GLCM) was performed on QUS parametric maps, resulting in quantitative measures of contrast (CON), correlation (COR), energy (ENE), and homogeneity (HOM) that reflects intra-tumor heterogeneity. Additionally, texture-derivate analysis was performed for each QUS parameter using a sliding window analysis to create textural images, from which second-pass "texture of texture" textural features were extracted from. Nine features were selected to train a machine learning algorithm identifying breast lesions as either “benign” or “malignant”. Three different classifiers including linear discriminant, k-nearest neighbors (KNN), and support vector machines (SVM) were implemented and evaluated.

Results: Among the biomarkers investigated, one mean-value, 16 textural, and 40 texture-derivate features showed statistically-significant differences ($p<0.05$) between the two lesion types. Among the different classifiers, KNN demonstrated the highest prediction results with a sensitivity=77%, specificity=72%, and accuracy=75%.

Conclusion: Mean-values of QUS parametric maps, along with texture and texture-derivates demonstrate a high potential for robust, noninvasive and accurate characterization of breast lesions. This work lays the foundations toward adapting novel QUS-based frameworks for breast cancer screening and rapid diagnosis in clinic.

1.2 **Early prediction of breast cancer therapy responses using quantitative ultrasound texture derivative method with machine learning approach**, Steven Brade, Lakshmanan Sannachi, Christopher Kolios, and Gregory Czarnota, *Department of Radiation Oncology, and Physical Sciences, Sunnybrook Health Sciences Centre, Sunnybrook Research Institute, Toronto, ON Canada, gregory.czarnota@gmail.com*

Background: Previous studies have demonstrated that combined quantitative ultrasound (QUS) and texture biomarkers are effective tools for monitoring locally advanced breast cancer patients (LABC) undergoing neo-adjuvant chemotherapy (NAC). In this study, we demonstrate the improvements in breast cancer response monitoring to NAC early after treatment using second derivative quantitative ultrasound texture features in conjunction with advanced machine learning methods.

Methods: Using a 6 MHz clinical ultrasound system, radiofrequency (RF) ultrasound data were acquired from 90 LABC patients prior to NAC treatment, and during the fourth week of treatment. Five QUS parametric images including mid-band fit (MBF), spectral slope (SS), spectral intercept (SI), average acoustic concentration (AAC) and average scatterer diameter (ASD) were determined from tumor RF data. For each QUS-image type four different texture images including contrast, correlation, energy and homogeneity were derived. Finally, four texture values were further derived from each QUS image (QUS-texture1) and QUS-texture image (QUS-texture2). Patients were classified into two groups based on ultimate clinical/pathological responses; responders and non-responders. Three machine learning algorithms were developed based on estimated parameters and evaluated.

Results: Classification algorithms developed using a support vector machine and *k*-nearest-neighbors methods could differentiate response groups with accuracies of 77% and 83%, and area under the receiver operating characteristic curve (AUC) values of 0.83 and 0.80, respectively. The most relevant features in separating the two response groups were QUS-texture2 features, particularly from AAC, SI, and MBF parametric images developed from pre-treatment tumor data. The 5-year recurrence free survival calculated for responder and non-responding patients based on a QUS-texture2 features model were comparable to those based on clinical-pathological outcome.

Conclusion: This study demonstrates for the first time that texture-derivative methods can be clinically applied to predict ultimate clinical and pathological responses of breast cancer patients early after the chemotherapy treatment. Future studies should examine the performance of this model in other populations and its subsequent utility in facilitating critical decisions of changing treatments for response-refractory patients early during treatment.

1.3 ***A priori* prediction of breast cancer response to neoadjuvant chemotherapy using quantitative ultrasound texture-derivative methods combined with machine learning**, Steven Brade, Lakshmanan Sannachi, Christopher Kolios, Gregory Czarnota, *Department of Radiation Oncology and Physical Sciences, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, gregory.czarnota@gmail.com*

Background: Responses of locally-advanced breast cancer (LABC) in the standard neoadjuvant chemotherapy (NAC) settings are often variable and the prediction of response is imperfect. Here, for the first time, we demonstrate the clinical utility of second derivative quantitative ultrasound texture features combined with machine learning in predicting the response to NAC administration prior to the start of the treatment.

Patient and Methods: A total of 100 LABC patients treated with NAC had breast tumors scanned with a 6 MHz clinical ultrasound system prior to chemotherapy treatment. Five quantitative ultrasound (QUS) parametric images were determined from ultrasound radio-frequency data within tumor regions of interest. For each QUS-image type four different GLCM (gray-level co-occurrence matrices) -based texture images were derived including contrast, correlation, energy, and homogeneity images using a sliding window approach. Finally, four texture values were further derived from each QUS image (QUS-texture1) and QUS-texture image (QUS-texture2). The ground truth labels for patients were classified into two groups based on ultimate clinical/pathological responses; responders and non-responders. Response classification was analyzed using a linear discriminant, a *k*-nearest-neighbors, and support vector machine classifiers and classification results were compared.

Results and Discussion: All algorithms distinguished responders and non-responders with prediction accuracy ranging between 62% and 90%. In particular, the *k*-nearest neighbors was the best classifier with values for sensitivity, specificity, accuracy, and area under the receiver operating characteristic curve (AUC) of 76%, 93%, 90%, and 0.81, respectively. The most relevant features in separating two response group were QUS-texture2 features from scatterer size and concentration-related parametric images. The 5-year recurrence free survival calculated for responder and non-responding patients based on the second derivative quantitative ultrasound texture features model were comparable to those based on clinical-pathological outcome.

Conclusion: The findings of this study suggest that second derivative quantitative ultrasound texture features of a breast tumor are strongly linked to tumor responsiveness. The pre-treatment assessment of tumor response could facilitate the change of ineffective treatments for refractory patients. Future work will include investigation into the ability of a second derivative quantitative ultrasound texture features based model in predicting patient recurrence free survival upon completion of chemotherapy and surgery.

2. ELASTICITY

2.1 **Longitudinal study of shear wave speeds in the human cervix during pregnancy,** Lindsey Carlson,[1,2] Helen Feltovich,[1,2] Timothy Hall,[2] [1]*Maternal Fetal Medicine, Intermountain Healthcare, Provo, UT,* [2]*Medical Physics, University of Wisconsin - Madison, Madison, WI, tjhall@wisc.edu*

Objective: In early pregnancy the cervix is a firm and helps hold the developing fetus in the uterus. At term the cervix has softened, shortened, and dilated to allow the fetus to pass through for vaginal birth. Clinical assessment of the softness of cervix is subjective. We have been developing objective measures of cervix softness and report here the results of a longitudinal study of shear wave speeds (SWS) in 30 women during pregnancy.

Methods: We recruited 21 multiparous and 9 nulliparous patients for serial transvaginal ultrasound exams. A linear array transducer was placed in contact with the cervix and positioned parallel to the cervical canal. Each individual was scanned at five timepoints (8-12 weeks, 14-18 weeks, 22-24 weeks, 32-34, and 37-39 weeks gestational age). Data were acquired using shear wave elasticity imaging pulse sequences on a clinical imaging system and data analysis was performed off-line.

Results: A linear mixed-effects model demonstrated that there is, as found ex vivo, a gradient in SWS along the length of the cervix. We found SWS decreases in humans from early to late pregnancy with a nearly constant fractional loss in SWS. These results are consistent with previously reported cross sectional studies in humans and with previously reported longitudinal studies in Rhesus macaque cervix.

Conclusions: These results suggest that may be an effective way to evaluate in the *in vivo* pregnant cervix. Supported by NIH grants F31HD082911 and R01HD072077 and the Intermountain Research & Medical Foundation. We are also grateful to Siemens Healthcare Ultrasound division for an equipment loan and technical support.

2.2 **Quality metric for multi-compression accumulated displacement estimates in nonlinear elasticity imaging**, Yuqi Wang, Timothy J. Hall, *Medical Physics Department, University of Wisconsin, Madison, WI*, wang636@wisc.edu

Background: The nonlinear elastic parameter of biological tissue can help differentiate breast disease and multi-compression is usually employed to generate the required large-deformation. To study the repeatability of nonlinear elastic parameter estimates, the procedure was performed for multiple scans on the same subjects. We report a method to measure the quality of the accumulated displacements among different multi-compression experiments within and among subjects.

Method: A series of small-strain compression steps were conducted on *in vivo* female breasts using a custom-built (constant incremental force) compression device and 2D radiofrequency (RF) echo data were acquired at each incremental step. The incremental displacements were estimated by a 2D companding motion tracking method that combines guided-search, regularized (block matching) displacement estimation for large-scale motion followed by a phase-tracking method for fine-scale motion. Then, these incremental displacements were mapped to the material points (with fixed coordinates) in the initial frame to obtain the accumulated displacements from the first step to each incremental step. The frame-average axial accumulated strain (AccStrain) at each step was computed from their accumulated displacements. To measure the quality of the accumulated displacements, the frame-average motion-compensated cross correlation between the first RF frame and each incremental frame (AccMCCC) was plotted against the AccStrain at that step (within and among subjects). Data providing a lower gradient in AccMCCC-vs-AccStrain were considered better data.

Results and Conclusion: Data quality judged by the AccMCCC-vs-AccStrain curve was consistent with subjective visual interpretation of the accumulated strain images. AccMCCC of at least 0.1 at AccStrain of 0.15 provided consistent accumulated strain images within subjects and the AccMCCC value at AccStrain of 0.10 was a useful index of motion tracking quality among subjects.

2.3 **Comparative study of PVCP and gel-oil elasticity phantoms for 3D printing**, Tara Diba[1], Nima Akhlaghi[2], Jason Zara[1], William Vogt[2], Timothy Hall[3], Brian Garra[2], [1]*Biomedical Engineering, George Washington Univ., Washington DC,* [2]*Office of Science & Engineering Labs, CDRH, FDA, Silver Spring, MD,* [3]*Medical Physics, Univ. of Wisconsin-Madison, Madison, WI. taradiba@gwmail.gwu.edu*

Ultrasound elastography (UE) is a noninvasive technique useful for measuring biological tissue stiffness. UE system testing using tissue-mimicking phantoms is essential for proper system characterization & calibration. An ideal phantom should possess the mechanical and acoustical properties plus the structural complexity of the tissue of interest. Current UE phantoms such as those simulating the breast are generally homogenous with simple inclusions, unlike heterogeneous breast tissue and irregular breast masses. 3D printing of printable tissue mimicking materials (TMM) has the potential to simulate the complexity of breast tissue. Three promising TMM are gelatin-oil,[(1)] polyvinyl alcohol (PVA)[(2)] and polyvinyl chloride plastisol (PVCP).[(3)] For 3D printing of complex multicomponent structures, the melting point, solidification speed on cooling (heat of fusion and heat capacity) and melted material viscosity determine if a material can be printed at proper spatial resolution with a given printer. Viscous materials and miscible materials must be printed using larger nozzle sizes resulting in lower spatial resolution and a less accurate representation of breast parenchyma.

The study goal is to evaluate the potential 3D printability of PVCP and gel-oil based TMM having tunable acoustic and mechanical characteristics similar to breast tissues. Elastic modulus of each material is measured by using a mechanical testing device (MicroTester, ADMET, Norwood, MA). Melting point and viscosity are estimated to determine suitability for printing. Finally, candidate materials are test printed using a two-component capable 3D printer (3D-Bioplotter, ENVISIONTEC, Dearborn, MI).

Two candidate materials have been tested yielding melting points of 38^{o} C (gelatin-oil) and 68^{o} C (PVCP). Qualitative viscosity tests show that the gelatin-oil material is much less viscous that the PVCP material. Printability testing is currently underway. Although both materials may be 3D printed, higher spatial resolution can be achieved with the gelatin-oil than the PVCP at the cost of decreased long-term stability.

(1) Madsen, EL, et al. *Ultrasound Med Biol 32*, 857-874 (2006). (2) Kharine, A, et al. *Phys Med Biol*, *48*, 357 (2006). (3) Vogt, WC, et al. *J Biomed Opt*, *21*, 101405 (2016).

2.4 **2D tracking improves quantitative nonlinear shear modulus estimation**, Soumya Goswami[1], Rifat Ahmed[1], Marvin M. Doyley[1,2], Stephen A. McAleavey[1,2], *Departments of [1]ECE and [2]Biomedical Engineering, University of Rochester, NY, sgoswam2@ur.rochester.edu*

Nonlinear shear elasticity imaging provides additional information about soft tissue and better contrast compared to linear elastic models. However, to observe the nonlinear behavior of tissue, large tissue strains are required. Estimation of nonlinear shear modulus (NLSM) with axial tracking alone ignores the lateral motion of tissue following higher deformation resulting in estimation errors and image artifacts. This work proposes to use a method of axial and lateral displacement tracking to estimate local axial strain with simultaneous measurement of shear modulus at multiple compression levels. By calculating the change in shear modulus versus the stress deduced from the measured strain, we obtain the nonlinear shear modulus. This method of 2D tracking produces NLSM images with 15-60% higher contrast ratio compared to axial tracking and contrast to noise ratio of 20 to 75 compared to 13 to 40 in 1D tracking. The SNR of the NLSM maps improved from 32 dB to 38 dB with the increase in cross-correlation coefficient of 2D tracking method from 0.94 to 0.99. Spatial variance in mean estimates of NLSM is reduced with 2D tracking (deviation of 4-8%) compared to axial tracking (deviation of 7-20%) in homogeneous phantoms. Results from inclusion phantoms of heterogeneous materials demonstrate that the behavior of nonlinear shear modulus with higher strain can be used to characterize different material properties. Additionally, we have validated our results with mechanically obtained nonlinear shear modulus measurements and the behavior of the NLSM is not significantly different from our method. Our method is less susceptible to variation in probe position and loading. For a lateral offset of 6 mm, we observe 2-4% variation in mean NLSM with 2D tracking vs 5-37% for 1D tracking. For an initial compression of 2.4 mm, the deviation in nonlinear shear modulus for our method is 3-6% compared to 10-15% for 1D tracking.

2.5 **Local phase velocity imaging (LPVI) for shear wave elastography of *in vivo* kidneys using a clinical scanner**, Piotr Kijanka[1,2], Matthew W. Urban[1,3], *[1]Department of Radiology, Mayo Clinic, Rochester, MN, [2]Department of Robotics and Mechatronics, AGH University of Science and Technology, Krakow, Poland, [3]Department of Physiology and Biomedical Engineering, Mayo Clinic, Rochester, MN, kijanka.piotr@mayo.edu*

Ultrasound-based shear wave elastography (SWE) provides measurements of various mechanical properties that can be used as diagnostic indicators in various clinical applications. Assessment of soft tissue viscoelastic parameters is of great interest in diagnosis of many diseases. Many clinical scanners measure the group velocity, or velocity with which the shear wave "packet" travels with time-of-flight methods. We present a clinical feasibility study of the Local Phase Velocity Imaging (LPVI) method (originally developed in (1)) used for the measurements of the viscoelastic properties of kidneys. The LPVI method creates maps of phase velocity for controlled, particular frequencies. The LPVI method involves directional and wavenumber filtering before applying various steps of Fourier-based operations to obtain localized maps of phase velocity over selected bandwidths. We will present an alternative implementation of the LPVI method to reduce the computation time more than 25 times. To evaluate the feasibility of translating LPVI for *in vivo* use, we used data acquired using a General Electric Logiq E9 in renal transplants in patients undergoing protocol biopsies. We reconstructed phase velocity maps for frequencies ranging from 80-350 Hz. We used the dispersion data and curve fitting to a Kelvin-Voigt model to estimate the shear elasticity and viscosity. We demonstrate feasibility of reconstructing maps of viscoelastic parameters in renal transplants with a fast implementation of LPVI based on 10 patients. This technique could be extended to other applications for evaluating images of viscoelastic mechanical properties.

(1) Kijanka P et al. *IEEE Trans Med Imaging* (2018). In press.

2.6 **Convolutional neural network for displacement and strain estimation for ultrasound elastography,** Md Golam Kibria, Andreas Bergdahl, Hassan Rivaz, *Electrical and Computer Engineering, Concordia University, Montreal CA, hrivaz@ece.concordia.ca*

Objective: Ultrasound elastography is a powerful yet inexpensive medical imaging tool that can provide valuable diagnostic information about tissue in real-time. Time delay estimation between two ultrasound echo signals before and after tissue deformation is the most critical part of ultrasound elastography. Time delay estimation can be considered a special case of optical flow estimation where structural continuity is present between two ultrasound images. Recently, Convolutional Neural Networks (CNNs) have shown promising results in optical flow estimation in real-time. We propose a method for robustly estimating displacement and strain in ultrasound elastography using CNN.

Methods: Our proposed method calculates displacement and strain from ultrasound echo signals in two phases. At first, we estimate a coarse displacement map using convolutional neural network which is robust as well as fast. The coarse displacement map is then refined using a global optimization based algorithm, GLUE[(1)]. This combination works well as GLUE relies on robust coarse displacement map for accurately calculation of displacement and strain.

Results: Our proposed method is validated using simulation phantom, experimental phantom and in-vivo patient data. Our method outperforms GLUE in terms of SNRe, CNRe, MSSIM and failure rate. Failure rate is calculated as the ratio of failed cases to total number of cases as an estimation of how likely the algorithm is going to fail. Our method shows very low failure rate (19.3548%, 04.8469%, 14.5408% and 60.7143%) compared to GLUE (58.0645%, 34.6939%, 68.3673% and 77.0408%) in experimental phantom and patients 1, 2 and 3 respectively.

Conclusions: A novel approach to estimate tissue displacement and strain from ultrasound images is introduced using CNN. The displacement estimation from CNN is further refined with GLUE. Our method is shown to be robust to decorrelation noise in simulation, experiments and *in-vivo* data. Supported in part by Natural Science and Engineering Research Council of Canada (NSERC) Discovery grant RGPIN-2015-04136. We would like to thank Microsoft Azure Research for a cloud computing grant and NVIDIA for GPU donation. The ultrasound data was collected at Johns Hopkins Hospital. The principal investigators were Drs. E. Boctor, M. Choti, and G. Hager. We thank them for sharing the data with us.

(1) Hashemi, HS, et al. *IEEE Trans Ultrason Ferroelectr Freq Contr 64*, 1625–1636 (2017)

2.7 **Physics-driven machine learning approach to quantitative 3-D quasi-static elastography**, Cameron Hoerig[1,2], Jamshid Ghaboussi[3], Michael F. Insana[1,2], *[1]Department of Bioengineering, [2]Beckman Institute of Advance Science and Technology, [3]Department of Civil and Environmental Engineering, University of Illinois at Urbana-Champaign, Urbana, IL 61801, hoerig2@illinois.edu*

Soft tissues exhibit complex material properties that are often changed by disease. Quasi-static ultrasonic elastography (QUSE) is sensitive to this mechanical contrast and may aid in the detection and diagnosis of disease. To create an image of material properties, most QUSE techniques invoke model-based inverse methods to estimate the parameter values of a preselected constitutive model. However, these methods are prone to modeling errors caused by selecting a constitutive model that does not accurately describe the mechanical behavior of tissue.

As a consequence, we developed a data-driven approach to QUSE using Cartesian neural network constitutive models (CaNNCMs) and the Autoprogressive Method (AutoP). AutoP utilizes finite element analysis to impose physical constraints on the material property distribution learned by CaNNCMs. Thus, from force-displacement measurements, CaNNCMs learn stress-strain behavior without a prior assumption of the underlying constitutive model.

Here, we demonstrate the ability of CaNNCMs to reconstruct the 3-D Young's modulus distribution of elastic materials from a sparse set of force-displacement measurements. We also introduce a new regularization term in AutoP that helps compensate for lack of information regarding the distribution of surface forces. With further development, CaNNCMs will be able to learn nonlinear and time-dependent material properties of tissues and allow for discovery of material parameters most relevant to clinical imaging.

Wednesday afternoon

3. IMAGING 1

3.1 **Tissue Doppler imaging to detect muscle fatigue**, Joseph Majdi, Siddhartha Sikdar, *Department of Bioengineering, George Mason University, Fairfax, VA, jmajdi2@gmu.edu*

Functional electrical stimulation (FES) is often used for rehabilitation in movement disorders and in assistive devices such as exoskeletons. However, FES can rapidly cause muscle fatigue, which limits the induced force production. At present, there exists no reliable, real time indicator for FES-induced muscle fatigue.

We believe that functional muscle physiology associated with muscle fatigue can be inferred from ultrasound imaging. In this study, we utilized tissue Doppler imaging (TDI) to quantify FES-induced twitch responses in the gastrocnemius muscle, at baseline and after inducing fatigue through repeated voluntary isometric contractions. We estimated muscle velocities using M-mode TDI to quantify differences in the twitch response before and after fatigue. Preliminary results

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indicate that fatigue induces a higher muscle acceleration during twitch, and the muscle contracts for a longer duration. These results could potentially be used as a real-time indicator for muscle fatigue. We are investigating the use of such a system integrated into an external hybrid walking exoskeleton that can switch from FES-induced force generation to external motors for force generation once the muscle fatigues. Further, it may be possible to replace TDI imaging with a wearable single-element continuous wave Doppler instrument for these measurements, reducing computational complexity and power requirements.

3.2 **Contrast plane wave Doppler imaging of the rat eye,** Ronald H. Silverman[1], Raksha Urs[1], Gulgun Tezel[1], Jeffrey A. Ketterling[2], Alfred C.H. Yu[3], Billy Y.S. Yiu[3], *[1]Department of Ophthalmology, Columbia University Irving Medical Center, New York, NY, [2]Riverside Research, New York, NY, [3]University of Waterloo, Waterloo, ON,* rs3072@cumc.columbia.edu

Background: We are developing the rat eye as an experimental model of glaucoma, an optic neuropathy associated with elevated intraocular pressure and impaired blood flow. In this report, we describe early results utilizing plane-wave Doppler imaging alone and after introduction of microbubble contrast agent.

Methods: We used a Verasonics Vantage-128 imaging system with an L22-14v linear array. Data were acquired from 6 angles over ±6º, providing 3000 compounded images per second for 1.5 sec. After initially acquiring scan data without contrast, 0.1 ml of 1:50 diluted USphere was introduced into the tail vein. We acquired data immediately and at 45 second intervals for 3 minutes. After beamforming and coherent addition, the data were processed using singular value decomposition and 10-Hz high-pass filters.

Results: The central retinal artery and vein as well as retina/choroid were evident in Doppler images prior to contrast, but dramatically brightened immediately after contrast injection, with the power Doppler signal roughly tripling in the first 1.5 seconds and peaking at the 45 second mark, after which it declined to baseline. Contrast enabled visualization of the choroidal arterioles, which were not evident without contrast.

Conclusions Plane wave ultrasound provides a means for imaging blood flow in the rat eye, which is just 7-8 mm in diameter. As rodents are widely used as models of ocular disease, we show the feasibility of using the rat for this purpose. We plan on evaluating perfusion by microbubble destruction and using superresolution techniques for improved spatial resolution of the microvasculature after interventions designed to increase intraocular pressure. Supported by NIH Grants EY025215, EY028550 and P30 EY019007 (Core Facilities for Vision Research) and an unrestricted grant to the Department of Ophthalmology of Columbia University from Research to Prevent Blindness.

3.3 **Proprioceptive sonomyographic control: A novel ultrasound-based method for prosthetic control for upper-extremity amputees**, Shriniwas Patwardhan[1], Biswarup Mukherjee[1,2], Ananya S. Dhawan[3], Nima Akhlaghi[1], Wilsaan Joiner[4], Siddhartha Sikdar[1,2], *[1]Department of Bioengineering, George Mason University, [2]Center for Adaptive Systems of Brain-Body Interface, George Mason University, [3]Department of Computer Science, George Mason University Fairfax,VA, [4]Department of Neurobiology, Physiology and Behavior, University of California, Davis, ssikdar@gmu.edu*

Background and Aims: Technological advances in multi-articulated prosthetic hands have outpaced the development of methods to intuitively control these devices. To overcome the limitations of the currently pervasive myoelectric control strategies, namely unintuitive proportional control of multiple degrees of freedom, we propose an ultrasound imaging based technique for sensing muscle activity, which we refer to as *proprioceptive sonomyographic control*. Unlike myoelectric control strategies our sonomyography-based strategy measures muscle deformation directly with ultrasound and uses the extracted signals to proportionally control the position of an end effector. Therefore, our sonomyography-based control is highly congruent with an amputee's innate proprioception of limb muscle deformation. In this work, we evaluate proprioceptive sonomyographic control with 5 amputee and 5 able-bodied participants in a virtual target achievement and holding task for 5 different hand motions and demonstrate its feasibility as a robust and intuitive prosthetic control strategy.

Methods: We recruited 5 able-bodied and 5 amputee subjects, one of whom is a congenital amputee to evaluate the accuracy of our sonomyographic control strategy. We asked the participants to perform predefined hand motions while ultrasound images of their forearm muscle movements are captured using a portable, commercial ultrasound system. We extract representative ultrasound images from the collected ultrasound data and perform leave-one-out validation to quantify prediction accuracy. Participants were then asked to perform the same hand motions in real-time while being shown an on-screen cursor that moves up or down in proportion to their muscle contract and relaxation respectively. A series of targets are presented at different levels of motion completion and the participant's ability to perform graded control to reach these targets using forearm muscle deformation is measured. Outcome metrics are position as a measure of the deviation of the desired and achieved position and stability error as a measure of the cursor jitter around the target.

Results: For the targets that were successfully acquired, able-bodied participants performed all motions except point with lower position and stability errors compared to amputee participants. Although, stability errors for able-bodied participants were lower than amputee participants, there seems to be a correspondence between motion-specific stability errors across participants. Motions with high stability errors in able-bodied participants also correspondingly have high stability errors in amputees. The type of motion also seems to have an influence on position errors and stability errors for all participants, i.e. motions with higher position error also have high stability error and vice versa.

Conclusion: We have developed an ultrasound-based sensing approach for detection of volitional user movement intent and extraction of proportional control signals in response to muscle deformations in the forearm. We tested our proposed *proprioceptive sonomyographic control* strategy using a visual cursor control task and demonstrated that amputee subjects are able to achieve accurate control of the cursor, with results comparable to able-bodied individuals. Our approach also enables true positional control of the end-effector device, as opposed to velocity control commonly implemented using myoelectric signals. This makes our system more intuitive to use and more directly congruent to the extent of muscle deformation that occurs during motion performance.

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Methods: We recruited 5 able-bodied and 5 amputee subjects, one of whom is a congenital amputee to evaluate the accuracy of our sonomyographic control strategy. We asked the participants to perform predefined hand motions while ultrasound images of their forearm muscle movements are captured using a portable, commercial ultrasound system. We extract representative ultrasound images from the collected ultrasound data and perform leave-one-out validation to quantify prediction accuracy. Participants were then asked to perform the same hand motions in real-time while being shown an on-screen cursor that moves up or down in proportion to their muscle contract and relaxation respectively. A series of targets are presented at different levels of motion completion and the participant's ability to perform graded control to reach these targets using forearm muscle deformation is measured. Outcome metrics are position as a measure of the deviation of the desired and achieved position and stability error as a measure of the cursor jitter around the target. *Results:* For the targets that were successfully acquired, able-bodied participants performed all motions except point with lower position and stability errors compared to amputee participants. Although, stability errors for able-bodied participants were lower than amputee participants, there seems to be a correspondence between motion-specific stability errors across participants. Motions with high stability errors in able-bodied participants also correspondingly have high stability errors in amputees. The type of motion also seems to have an influence on position errors and stability errors for all participants, i.e. motions with higher position error also have high stability error and vice versa.

Conclusion: We have developed an ultrasound-based sensing approach for detection of volitional user movement intent and extraction of proportional control signals in response to muscle deformations in the forearm. We tested our proposed *proprioceptive sonomyographic control* strategy using a visual cursor control task and demonstrated that amputee subjects are able to achieve accurate control of the cursor, with results comparable to able-bodied individuals. Our approach also enables true positional control of the end-effector device, as opposed to velocity control commonly implemented using myoelectric signals. This makes our system more intuitive to use and more directly congruent to the extent of muscle deformation that occurs during motion performance.

3.4 **Safety and acoustic output characterization of a time delay spectrometry based ultrasound imaging system**, Biswarup Mukherjee[1], Ananya S. Dhawan[2], Elizabeth Tarbox[1], Nima Akhlaghi[2], Paul Gammell[3], Parag Chitnis[1], Siddhartha Sikdar[1], *[1]Department of Bioengineering, George Mason University, Fairfax, VA, [2]Department of Computer Science, George Mason University, Fairfax,VA, [3]Gammell Applied Technologies LLC, Exmore, VA,* ssikdar@gmu.edu

Background and Aims: Clinical ultrasound systems utilizing pulse-echo imaging require high voltage and short duration transmit pulses along with electronics that operate in the MHz frequency range. We have developed an imaging method based on time-delay spectrometry (TDS) that employs a low-voltage, wideband, chirp transmit signal to establish a relationship between time of flight of the signal, thus depth, and transmit frequency. In previous years, we reported a TDS system with a separate transmit and receive chain which requires a dual element transducer to operate. In this work, we build on the TDS paradigm and demonstrate a system with a combined transmit and receive signal path that can be used with commercial single element transducers. Furthermore, we characterize the acoustic output parameters for the TDS system to establish its safety for clinical imaging purposes and demonstrate the ability to dynamically image deep-seated tissue in real-time.

Methods: The TDS system consists of an AD5930 swept-frequency source (250 kHz/ms, ±4.5$V_{p\text{-}p}$), a custom RF transmit amplifier to boost the chirp signal, a diode-based passive demodulator for TDS mixing, and a receive amplifier/ low-pass filter. The resulting down-mixed signal is digitized by a data acquisition system and processed in MATLAB. A commercially available 4.25 MHz single element transducer was used characterize the acoustic output characteristics. Beam profiles were scanned using a 3-axis linear motor stage and a Onda HNA-0040 hydrophone. *Results:* For the TDS system, peak negative pressure was found to be 71 kPa which produced a spatial peak, temporal average intensity value of 37.6 mW/cm^2, in water, well below the derated FDA limit of 94 mW/cm^2. Mechanical index (MI) was found to be 0.041. Thermal indices for soft tissue, bone and cranium were 0.02, 0.24 and 0.14 respectively, well below the 0.7 FDA limit for continuous, long term use. With these TDS drive parameters, we obtained *in-vivo*, M-mode images with average CNR of 32 dB and successfully tracked muscle-tissue boundaries for imaging depth up to 4 cm, in real-time at frame rates of approximately 50 Hz.

Conclusion: We demonstrate the utility of time delay spectrometry-based ultrasound imaging systems for real-time, *in-vivo* ultrasound imaging applications. Acoustic safety characterization of TDS shows that for MI and TI values are well below FDA limits. With this TDS system, we successfully imaged multiple tissue interfaces in real-time with high CNR, making it ideal for use in long term monitoring and wearable applications.

4. IMAGING 2

4.1 **Fast subsample speckle tracking method based on normalized cross correlation**, Brandon Rebholz, Mohamed Almekkawy, *School of Electrical Engineering and Computer Science, The Pennsylvania State University, University Park, PA,* bpr5072@psu.edu

Background: Accurate displacement estimation is a vital foundation for many fields in ultrasound imaging, such as elastography or blood flow estimation. Normalized cross correlation (NCC) is well known to generate accurate displacement estimates, however, the accuracy is limited to the sample level. Due to the low lateral resolution in ultrasound images, this presents a problem for subsample estimation. In order to generate subsample estimates, interpolation is performed on the correlation map generated by NCC. This was seen, however, to not be analogous in accuracy to interpolating a B-Mode image before NCC. We propose a method that interpolates in a specific area for each point, thereby drastically reducing the computational time, while maintaining the subsample accuracy. This method will be referred to as Targeted B-Mode Interpolation (TBI).

Methods: TBI first correlates on the sample level and finds the maximum point. The B-Mode image is interpolated in a constrained region within one pixel around the maximum correlation point and correlation is recalculated with an interpolated reference kernel to find the peak with subsample accuracy. Interpolating the entire image and interpolating the correlation map will be referred to as General B-Mode Interpolation (GBI), and Correlation Upsampling (CUS), respectively.

Results and Conclusion: Tests were performed on two data sets generated by Field II. The two sets include parabolic laminar blood flow data where the peak displacement is 0.8 and 4 pixels respectively. Mean squared error is as follows for 0.8 peak data: CUS (0.0358), GBI (0.0048), TBI (0.0070). For the 4 pixel peak data: CUS (0.0363), GBI (.0282), TBI (.0264). TBI executes on the same timescale as CUS, while GBI took 240X the time. TBI and GBI are more accurate than CUS, however TBI executes drastically faster than GBI with comparable accuracy. This method has additionally generated valid strain images on an elastography phantom.

4.2 **Ultrasound-waveform tomography using speckle diffraction,** Lianjie Huang, Benxin Chi, Kai Gao, Yunsong Huang, *Los Alamos National Laboratory, Los Alamos, NM 87545, ljh@lanl.gov*

Ultrasound-waveform tomography is used to reconstruct tissue mechanical properties for cancer characterization. For many ultrasound imaging applications, no transmission ultrasound data are available for ultrasound tomography, but only ultrasound reflection/scattering data are available, such as transrectal ultrasound tomography. We develop a novel ultrasound-waveform tomography/inversion method using speckle diffraction to significantly improve ultrasound tomographic reconstruction using a single transducer array. Ultrasound data contain significant speckle diffraction. We use wide-beam, fan-beam, or plane-wave ultrasound to enhance ultrasound diffraction, which illuminates targets of interest such as tumors from different directions. We use these ultrasound signals for ultrasound-waveform inversion to reconstruct tissue sound-speed values. We verify our method using phantom data acquired using our transrectal ultrasound tomography prototype consisting of a 256-channel Verasonics Vantage system and a GE intracavitary curved linear array. Our phantom imaging results demonstrate that our new ultrasound-waveform tomography using speckle diffraction has potential to accurately reconstruct sound-speed values of prostate tumors using a transrectal ultrasound array.

4.3 **Adaptive clutter subtraction in B-mode imaging using lag-one coherence (LOC)**, Will Long[1], Nick Bottenus[1], Gregg E. Trahey[1,2], *Departments of [1]Biomedical Engineering and [2]Radiology, Duke University, Durham, NC, willie.long@duke.edu*

Spatial coherence, describing the correlation of received channel signals as a function of element separation (i.e. lag), is sensitive all major forms of clutter. For spatially incoherent clutter, such as reverberation and thermal noise, the superposition of uncorrelated noise on partially correlated signal results in a step discontinuity in the coherence function at the shortest lag.

We have developed an imaging metric, termed the lag-one coherence (LOC), which captures the magnitude of this discontinuity using the average correlation between adjacent channels. LOC has been shown to provide a reliable measure of clutter in realistic imaging conditions, and under certain assumptions, can be directly related to the channel signal-to-clutter ratio.

In this study, we extend the application of LOC to adaptive beamforming and present a novel method in which measurements of LOC are used to adaptively estimate and remove the contribution of additive incoherent clutter from beam-summed pixel intensity. We compare this method to DAS and other adaptive beamformers in Field II using simulated lesions of varying native contrast over a range of channel noise levels. Examples images from 10 *in vivo* liver and fetal datasets are evaluated and discussed.

For a simulated -12 dB lesion, LOC clutter subtraction preserves intrinsic target contrast at channel SNRs roughly 15 dB worse than DAS. Texture SNR with clutter subtraction maintains DAS Rayleigh statistics for SNRs above 0 dB. At higher noise levels, decreases in texture SNR are coupled with gains in contrast that lead to net increases in both CNR and GCNR over DAS. Similar trends are observed in *in vivo* images, which show contrast and CNR improvements between 0.3-7 dB and 1.7-20%, respectively. LOC clutter subtraction shows promise to mitigate image degradation by clutter, while preserving the texture and contrast characteristics of conventional B-mode imaging.

4.4 **Characterization of *in-vivo* human breast tumors using Harmonic Motion Imaging (HMI) -- Initial clinical feasibility,** Niloufar Saharkhiz[1], Hermes Kamimura[1], Rachel Weber[1], Bret Taback[2], Richard Ha[3], Elisa Konofagou[1,3], [1]*Department of Biomedical Engineering, Columbia University, NY,* [2]*Department of Surgery, New York-Presbyterian Hospital, NY and* [3]*Department of Radiology, Columbia University, NY, ek2191@columbia.edu*

Background and objective: Noninvasive assessment of tissue mechanical properties can potentially diagnose breast cancer and reduce the number of biopsies. Our group has recently shown the capability of Harmonic Motion Imaging (HMI) in differentiating tissues with variable stiffness of post-surgical human breast specimens. In this study, we apply HMI to patients with breast masses *in-vivo* to assess clinical HMI feasibility and initial differentiation between benign and malignant tumors.

Methods: A 4-MHz Focused Ultrasound (FUS) transducer generated an amplitude-modulated acoustic radiation force (AM frequency: 25 Hz) to induce tissue displacements. A 2.5-MHz phased array probe confocal with the FUS transducer was used to simultaneously image the tissue through a Verasonics Vantage system at 1000 frames s^{-1} using a plane-wave sequence. The channel data was then reconstructed using a delay-and-sum algorithm and the harmonic displacements were estimated using 1-D cross correlation. Breast masses were first identified on B-mode images followed by an in-plane, 1-D HMI raster scan using a robotic arm at a step of 2-3 mm. Six female patients (age: 68 ± 17 years) with breast masses were recruited.

Results: The axial peak-to-peak displacement amplitudes were used to reconstruct a 2-D HMI displacement map. The size and location of the tumors were correlated with the B-mode images. In each HMI map, the displacements were averaged in a region of interest (ROI) defined on the B-mode image within the breast tumor and surrounding tissue. The average HMI displacement was found to be equal to 0.51 ± 0.08 µm in malignant tumors (n=3), 2.37 ± 0.09 µm in benign tumors (n=2) and 3.61 ± 1.41 µm in the perilesional tissue (n=6).

Conclusion: This initial clinical application of HMI in breast cancer patients demonstrates its clinical feasibility and potential for the noninvasive differentiation of benign from malignant breast tumors and from normal breast tissue.

5. NIH PROGRAM FUNDING

Thursday morning

6. IMAGING/ROBOTICS

6.1 **Robotic hand-over-hand control framework for transabdominal ultrasound with implications for co-robotic ultrasound tomography guided by endorectal probe,** Kevin Gilboy[1], Yixuan Wu[1], Mahya Shahbazi[2], Russell Taylor[3], Emad Boctor[3-4], [1]*Dept. of Electrical and Computer Engineering,* [2]*Laboratory for Computational Sensing and Robotics,* [3]*Dept. of Computer Science,* [4]*Dept. of Radiology, Johns Hopkins University, Baltimore, MD, kevingilboy@jhu.edu*

The combination of ultrasound (US) imaging with robotics has ushered in a new realm of imaging capabilities, but little focus has been placed on the methods for maneuvering the probe from bedside to patient. While easily overlooked, this is an important first step for conducting any robot-assisted US procedure and can also be employed to reduce the physical exertion of sonographers by providing them with probe “power-steering” functionality as they guide the probe and hold it against a patient with high force.

The goal of this work is to develop an extensible, cooperatively controlled robotic assist software framework for an US probe-wielding robot with initial implications in alleviating sonographer work-related musculoskeletal issues while also increasing image quality through enforced probe stability that nullifies the effects of tremor and hand readjustments on the image. The framework, utilizing nonlinear admittance control algorithms operating on dual-force sensors and inferences made by an adaptive Kalman filter, aims to provide sonographers with smooth, intuitive control that also optionally obeys specified virtual fixtures and patient-probe force limits.

The resulting software framework will be tested against the traditional freehand scanning method in a wide user study that quantifies reduced sonographer physical exertion through surface EMG sensing, as well as perceived difficulty, strenuousness and dexterity assessed through task load questionnaires. The images acquired during this study will also be analyzed for improvements in image stability versus the freehand method, which would be a significant development for synthetically tracked aperture imaging, US tomographic reconstruction and enforcing steady imaging during biopsies. With the success of these results, future work will be aimed at a novel co-robotic application of this framework to US tomography of the prostate for diagnosis, in which a robot-held transabdominal probe will track the rotations of a freehand transrectal probe to capture an array of transmission US images necessary for tomographic reconstruction.

6.2 **Autonomous robotic ultrasound scanning with six-degree-of-freedom force feedback control**, Jakub T. Kaminski[1], Haichong K. Zhang[1,2], *[1]Robotics Engineering, [2]Biomedical Engineering, Worcester Polytechnic Institute, Worcester, MA, hzhang10@wpi.edu*

Classical medical ultrasound procedures are performed manually by an occupational operator with a hand-held ultrasound probe. These procedures require high physical and cognitive burden and yield clinical results that are highly operator-dependent. A robotic ultrasound procedure, on the other hand, is an emerging paradigm integrating a robotic arm with an ultrasound probe and it achieves an automated ultrasound scanning by controlling the scanning trajectory and the contact force, thus making the procedure more informative and comparable in subsequent examinations over a long time span. As the state of the art, Kojcev et al. has reported the use of sensor-tissue normal contact force measured by a 1-DoF sensor to maintain the force applied to the tissue from the probe. In this work, we present a novel robotic ultrasound platform featuring a 7-DoF robotic arm equipped with a 6-DoF force-torque sensor coupled to an ultrasound probe. The measured forces and torques affecting on the probe are used to adaptively modify the predefined trajectory during autonomously performed examinations. We evaluated multiple scanning configurations in subsequent trials over pre-planned path completed on a tissue-mimicking phantom and the repeatability of the ultrasound scan was assessed by quantitatively comparing ultrasound images within multiple trials. In addition, automated scanning with 3D force sensing can generate a 3D map of the phantom surface and that was compared with the actual geometry of the phantom to validate the sensitivity of multi-DOF sensing.

6.3 **Modular ultrasound for needle guidance: a hands-free approach**, Keshuai Xu[1,2], Christian A. Hernandez[3], Younsu Kim[1,2], Haichong K. Zhang[4,5], Emad M. Boctor[1,2,6], *[1]Dept. of Computer Science, [2]Laboratory for Computational Sensing and Robotics, [3]Dept. of Biomedical Engineering, Johns Hopkins University, Baltimore, MD, [4]Dept. of Biomedical Engineering, [5]Robotics Engineering, Worcester Polytechnic Institute, Worcester, MA, [6]Dept. of Radiology, Johns Hopkins University, Baltimore, MD, keshuai@jhu.edu*

The form factors of medical ultrasound imaging systems have been shrinking over the last five decades due to miniaturization of electronics and advancement in processing power: from cart-based systems in the 1970s to laptop-based in the 1990s, then to tablet- and phone-based in the 2000s. The current generation ultrasound systems optimize for hand-held probes operated by sonographers but are often cumbersome and disruptive for image-guided procedures and impractical for continuous monitoring. We envision the next generation of medical ultrasound devices -- a patch that attaches to the patient without the need for a human or robot hand to hold. The ultrasound patch contains single element or small aperture modules integrated with acquisition and processing electronics. We present a lumbar puncture guidance "patch" that utilizes a moving phased array to demonstrate the potential of this new framework. Lumbar puncture is a traditionally "blind" procedure with over 23% failure rate and is especially challenging with obese patients. We move a 64-element phased array on a linear rail to enable imaging the interspinous space with multiple insonification angles to visualize the bone structure around needle path, which is mostly shadowed under a linear array or a stationary phased array. We acquire multiple B-mode sector images along the linear rail and compound the images based on bone probability determined by intensity and shadow. Results show improved visibility of the spinous process bone structure that defines the needle insertion path, and the image quality is not sensitive to lateral placement of the patch. Other applications of this patch-based moving phased array can potentially expand to catheter guidance and advanced ultrasound imaging techniques.

6.4 **Phantom for simulating multi-modality imaging in transcatheter interventions**, Michael A. Speidel,[1,2] Lindsay E. Bodart,[1] Martin G. Wagner,[1] Amish N. Raval,[2] Timothy J. Hall[1], *Departments of [1]Medical Physics, [2]Medicine, University of Wisconsin – Madison, speidel@wisc.edu*

Background: A growing class of structural heart interventions require deployment of catheter-based devices within relatively large three-dimensional chambers and vessels. Co-registered x-ray fluoroscopy and echocardiography is a potential solution for the real-time visualization of the device and its soft tissue context. We present a novel phantom that can be used to evaluate registration accuracy in these emerging technologies or to simulate multi-modality imaging in transcatheter interventions.

Methods: The phantom consisted of a plastic outer shell, swappable inserts containing objects for imaging tests, and an ultrasound-compatible, tissue-mimicking fluid medium filling the space between the insert and the outer shell. Access ports were added for insertion of devices and invasive imaging probes (e.g. TEE), and acoustic windows provided coupling for TTE probes. The window geometry was informed by 3D measurements of TTE probe positions on human subjects. An insert for testing x-ray/echo co-registration was created by embedding custom-fabricated dual-modality spherical targets in an anechoic agar insert. To demonstrate x-ray/echo imaging of a TAVR valve, a hollow insert with agar-graphite wall and water-alcohol core was constructed. The phantom was imaged with bi-plane x-ray angiography, echocardiography, and CT.

Results and Discussion: The co-registration test insert contained a helix of 24 spherical agar targets (5 mm diameter) with 150 mg/mL barium sulfate for x-ray contrast and 100 mg/mL glass microbeads (55-63 m) for echo signal. Dual-modality target contrast was 16% in x-ray fluoroscopy (90 kV) and target CNR relative to the fluid medium was 4-4.3 in ultrasound images acquired at a center frequency of 2.8 MHz. No reverberation artifacts were observed from the walls of the enclosure. Target visualization under x-ray and ultrasound was sufficient to enable calculation of 3D target registration error in co-registered x-ray/echo images.

Conclusion: A customizable phantom suitable for testing x-ray/echo co-registration algorithms and simulating multi-modality device imaging has been constructed.

7. PHOTOACOUSTICS

7.1 **Contrast-enhanced spectroscopic photoacoustic imaging of prostate cancer using fluorescence-quenching prostate-specific membrane antigen (PSMA)-targeted contrast agent**, Jeeun Kang[1], Yixuan Wu[2], Ala Lisok[3], Haichong K. Zhang[1], Martin G. Pomper[3], Sangeeta Ray[3], Emad M. Boctor[1-3], *[1]Department of Electrical and Computer Engineering, [2]Department of Computer Science, The Johns Hopkins University, Baltimore, MD, [3]The Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins Medical Institutions, Baltimore, MD, kangj@jhmi.edu*

Sensitive, noninvasive imaging of primary prostate cancer (PC) is important for early detection and could benefit patients undergoing active surveillance. Here, we present contrast-enhanced prostate-specific membrane antigen (PSMA)-targeted spectroscopic photoacoustic (sPA) imaging. A PSMA-targeted contrast agent conjugated with multiple near-infrared fluorescence dye molecules, IRDye800CW, was introduced to enhance PA contrast as a reciprocal gain of fluorescence quenching. *In vitro* experiments were conducted using the isogenic $PSMA^+$ PC3-PIP and $PSMA^-$ PC3-flu model system. Multi-wavelength PA data were collected with a tunable Nd:YAG optical parametric oscillator (OPO) laser system (Phocus Inline, Opotek, Inc., United States) and ultrasound research package (Vantage 256, Verasonics, Inc., United States). Theoretical analysis from spectrophotometry and spectrofluorometry on phantom-tubing data indicated 164.7-fold lower quantum yield from the original IRDye800CW contrast when tested at the same molar concentration (10 µM), leading to 8.7-times higher PA contrast at 780 nm for the targeted, multi-scaffold dye. Also, the targeting specificity of the complex to PSMA was validated with 2.94-times higher PA intensity with the $PSMA^+$ PC3-PIP cell suspension than that due to the suspension of $PSMA^-$ PC3-flu cells: 1.00±0.07 vs. 0.34±0.02 of normalized PA intensities, respectively. These results indicate the feasibility of PSMA-targeted fluorescence quenching contrast for sPA imaging. Future work will involve advanced signal processing for noninvasive, high-contrast characterization of deep PC *in vivo*.

7.2 **Photoacoustic imaging of signals from a custom drill tip inside a human vertebra with coherence-based beamforming,** <u>Eduardo Gonzalez,</u>[1] Alycen Wiacek,[2] Muyinatu A. Lediju Bell,[1-3], ***[1]****Departments of Biomedical Engineering,* ***[2]****Electrical and Computer Engineering,* ***[3]****Computer Science, Johns Hopkins University, egonza31@jhmi.edu*

During spinal fusion surgeries, the surgeon places screws through the pedicles of vertebrae in order to connect them with a metal rod and stabilize the spine to normal function. Outstanding challenges with this procedure include finding the starting point for screw insertion into the pedicle, and ensuring that a drill tip maintains the correct trajectory when drilling pilot holes for screw insertion. We demonstrate a photoacoustic imaging system for drill tip tracking that will co-register photoacoustic images with pre-operative CT acquisitions, relying on two innovations in system designs and signal processing techniques. First, a novel drill bit design containing an optical fiber inside a hollow core was inserted into a pre-drilled hole in the pedicle of an *ex vivo* human vertebra. The first 13 mm of the 32mm-deep pre-drilled hole corresponded to the pedicle and the remaining 19 mm extended into the vertebral body. Data were acquired using a Phocus Mobile (Opotek, Inc.) laser at 760nm wavelength with energies of 1.0 mJ, 2.2 mJ and 3.4 mJ at the fiber tip. Second, the signal was tracked with low localization error (1.0 ± 0.8 mm) at 0-6 mm insertion depths into the pedicle, with a high SNR of 59.0 ± 28.9 when using a novel coherence-based beamformer named Locally Weighted Short-Lag Spatial Coherence.[(1)] For comparison, conventional delay-and-sum beamforming produced a significantly lower SNR of 8.2 ± 5.8. Challenges include reduced SNR and increased localization errors beyond 6 mm insertion depth. In addition, strong artifacts appeared at insertion depths of 28-35 mm, due to sound reflections within the vertebral body. These results are a promising start that warrant further investigation into this new technological area of photoacoustic-guided spinal fusion surgeries.

(1) Gonzalez, E. et al. in *Proc IEEE International Ultrasonics Symp* (2018).

7.3 **Additive noise models for simulated photoacoustic coherence-based imaging**, Brooke Stephanian[1], Michelle T. Graham[2], Huayu Hou[2], Muyinatu A. Lediju Bell[1,2], [1]Department of Biomedical Engineering, [2]Department of Electrical and Computer Engineering Johns Hopkins University, Baltimore, MD, mledijubell@jhu.edu

Short-lag spatial coherence (SLSC) imaging is a beamforming method which is useful for improving contrast in high-noise imaging situations. The advantages of SLSC imaging over traditional delay-and-sum beamforming was previously demonstrated with photoacoustic imaging experiments. The goal of this research is to develop noise models that enable more accurate simulations of coherence functions which form the basis of coherence-based photoacoustic imaging. Two models were developed based on experimental observations of noise.(1) First, we observed that randomness in coherence estimates appears to be independent of lag. Second, the lag-one coherence value was observed to be significantly lower than the lag-zero value when imaging with low-energy pulsed laser diodes. Random noise was modeled by adding random values from a zero-mean, normal distribution to theoretical spatial coherence functions. Low-energy laser noise was modeled as a scaled delta function. When comparing theoretical spatial coherence image without noise to *in vivo* data, there were large differences in contrast, signal-to-noise ratio (SNR), and contrast-to-noise ratio (CNR), specifically 6.0 dB, 9.9, and 7.7, respectively. Accuracy increased when the noise models were included, resulting in contrast, SNR, and CNR differences of 2.7 dB, 0.1, and 1.5 respectively, when comparing the simulations with noise to *in vivo* data. This increased accuracy due to the inclusion of the additive noise models is promising for future optimization of coherence-based photoacoustic imaging methods.

(1) Stephanian B, et al. *Biomed Opt Exp 9*, 5566-5582 (2018).

7.4 **Pixel-wise deep learning for improving image reconstruction in photoacoustic tomography**, Steven Guan, Amir A. Khan, Siddhartha Sikdar, Parag V. Chitnis, *George Mason University, Fairfax, VA, Sguan2@gmu.edu*

Photoacoustic tomography involves absorption of pulsed light and subsequent generation of ultrasound, which when detected using an array of sensors can produce clinically useful images. Practical considerations limit the number of sensors as well as their “view” of the region of interest (ROI), which can result in significant reconstruction artifacts. Iterative-reconstruction methods can improve image quality but are computationally expensive. Another approach to improve reconstructed images is to use convolution neural networks (CNN) as a post-processing step for removing artifacts. However, missing or heavily obscured features typically cannot be recovered using this approach. We present a new pixel-wise deep learning (PDL) approach that employs pixel-wise interpolation to window ROI-specific raw photoacoustic data and then directly performs the image reconstruction within the CNN framework. The utility of this approach was demonstrated on simulated photoacoustic data from a 64-element semi-circular sensor array. The training and testing datasets comprised of 500 images from a synthetic vasculature phantom and 50 images of an anatomically realistic vasculature obtained from micro-CT images, respectively. Structural similarity index (SSIM) of the PDL-reconstructed images (0.91±0.03) indicated superior image quality compared to those obtained using the iterative reconstruction (0.82±0.09) and CNN-based artifact removal (0.79±0.07).

Thursday afternoon

8. ARFI

8.1 **Combining 3D ARFI, SWEI, B-mode, and QUS to improve identification of prostate cancer,** D. Cody Morris[1], Derek Y. Chan[1], Hong Chen[2], Mark L. Palmeri[1], Thomas J. Polascik[3], Jonathan Mamou[2], Kathryn R. Nightingale[1], [1]*Biomedical Engineering, Duke University, Durham, NC,* [2]*Lizzi Center for Biomedical Engineering, Riverside Research, New York, NY,* [3]*Department of Surgery, Duke University Medical Center, Durham, NC, cody.morris@duke.edu*

Background: In an ongoing study, a transrectal ultrasound prostate system capable of acquiring 3D ARFI, SWEI, B-mode and QUS data *in vivo* was used to acquire RF data from six subjects to date scheduled to undergo radical prostatectomy. Post-prostatectomy whole mount histology was utilized as the gold standard to quantify the performance of each individual or combination of ultrasound methods at identifying prostate cancer (PCa). The goal of this study was to determine the improvement in PCa identification gained by combining multiple ultrasonic techniques.

Methods: Co-registered ARFI/SWEI elasticity and B-mode/QUS data were captured using custom sequences on a Siemens SC2000 with an Acuson ER7B side-fire transducer rotated with 1 degree elevational spacing to obtain the 3D image volumes. ARFI and SWEI data were processed using state of the art techniques described by Palmeri[(1)] and Song.[(2)] The QUS parameters were calculated with a phantom based reference spectrum as described by Oelze.[(3)] The index lesion and a healthy region were manually segmented in each dataset based on ARFI and B-mode image appearance using visual confirmation with cognitively registered whole mount histology. These segmentations were applied to the SWEI and QUS volumes to obtain values at each matching voxel. Linear discriminant analysis was used to combine parameters from these techniques and receiver operating characteristic (ROC) curve analysis was used to assess differentiation between PCa and healthy tissue.

Results/*Discussion*: Individually the four techniques yielded areas under the ROC of 0.95 for ARFI, 0.74 for B-mode, 0.77 for SWEI, and 0.75 and 0.84 for the QUS intercept and midband fit, respectively. By combining subsets of these techniques, the AUROC rose to 0.83 for B-mode and SWEI, to 0.85 for B-mode and QUS, and 0.89 for SWEI and QUS. Combining all four imaging techniques the AUROC rose to 0.96. This work demonstrates the improvement in PCa detection gained by combining modalities which paves the way for a combined method for automatic PCa detection and targeted biopsy. Supported by NIH grants R01CA142824, R03EB026233 and DOD PCRP award W81XWH-16-1-0653

(1) Palmeri, *UMB* (2016). (2) Song, *UMB* (20140. (3) Oelze, *IEEE UFFC* (2016).

8.2 **Toward frequency-dependent modulus reconstruction from ARFI wave fields**, Sanjay Yengul, Olalekan Babaniyi, Paul E. Barbone, *Mechanical Engineering, Boston University, Boston, MA.* barbone@bu.edu

Ultrasound shear wave elastography (SWE) aims to quantify tissue properties from measurements of propagating shear wave fields. Often, those shear waves are excited by acoustic radiation force (ARF). Here, we consider several issues that must be resolved en route to the overall goal of quantifying tissue mechanical properties in ARF-SWE. First is identifying an appropriate mathematical model for ARF excited shear wave propagation. To that end, we validate an axisymmetric viscoelastic model suitable for some applications of acoustic radiation force imaging. This model is in the frequency domain, and it shows the importance of the vector nature of the shear wavefield. This motivates the second problem, which is to reconstruct lateral displacement components from measured axial displacement components. To that end, we evaluate an approach utilizing tissue incompressibility. Third, given measured displacement vector fields in the body, we seek to recover the viscoelastic property distribution on a frequency by frequency basis. To that end, we present a new inverse problem formulation for the axisymmetric, time-harmonic, viscoelastic, vector wave equation. The direct error in constitutive equation formulation relies on minimizing the error in the constitutive equation with a momentum equation constraint. This method requires no computational iteration and so runs almost instantly. Numerical results on simulated data show that the formulation is capable of handling discontinuous and noisy strain fields and also converging with mesh refinement for continuous and discontinuous material property distributions. Applications to ultrasound measured ARF wave data are considered.

8.3 **Regularized shear wave speed reconstruction with an on-axis ARFI-based prior**, Derek Y. Chan, Ned C. Rouze, Mark L. Palmeri, Kathryn R. Nightingale, *Department of Biomedical Engineering, Duke University, Durham, NC, derek.chan@duke.edu*

Introduction: Shear wave elasticity imaging (SWEI) tracks the speed of shear waves in tissue to provide quantitative stiffness information. SWEI image quality is often degraded by noisy estimates due to low shear wave amplitudes or by poor spatial resolution as a result of the reconstruction kernel size. On the other hand, acoustic radiation force impulse (ARFI) imaging tracks the on-axis displacement within the region of excitation. Though it measures only relative stiffness, ARFI typically has greater resolution and depth penetration than SWEI.

The distinct advantages and challenges associated with each of these techniques suggest that simultaneously-obtained ARFI and SWEI data may be combined for enhanced accuracy and resolution. We present a novel framework for improving the quality of shear wave elasticity images with Bayes' theorem, using a prior distribution based on local ARFI stiffness information.

Methods: A likelihood function is implemented for the shear wave arrival time estimation problem, based on cross-correlation of the particle velocity signals at off-axis track locations. The weighted-average algorithm incorporates data from multiple push excitations for a more robust calculation. A prior distribution for the arrival time is formulated using expected relations between shear wave speed, shear modulus and particle displacement magnitude from the ARFI data. Maximizing the resulting posterior distribution results in the set of arrival time estimates that is most consistent with both the observed shear wave velocity profiles and the expected relative stiffness differences.

Results: For combined ARFI/SWEI data obtained in a phantom with a stiff inclusion, the proposed estimator resulted in a SWEI reconstruction with greater depth penetration and improved the lesion edge resolution by 20% compared to conventional SWEI. The impact of noise is evaluated through variable weighting of the likelihood and prior distributions.

Improved SWEI estimation is demonstrated in an *in vivo* human prostate dataset, for which shear wave imaging conditions are particularly challenging.

8.4 **Assessing lag-one coherence as a tool for ARFI bias estimation**, James Long, Anna Knight, Gregg Trahey, Kathryn Nightingale, *Department of Biomedical Engineering, Duke University, Durham, NC, james.long5@duke.edu*

Introduction: The efficacy of ARFI as a clinical tool is hindered by sources of noise that affect the accuracy of displacement estimation. Acoustic clutter generated by reverberation and phase aberration introduced in the abdominal wall is temporally stable and produces an overlaying pattern that has zero displacement through time.(1) Because of this, estimated displacements are often biased towards zero due to tracking of the stable pattern. We propose to use lag-one coherence (LOC),(2) a validated measure of clutter levels, to predict displacement bias, and we hypothesize this information can be used to remove the effects of bias in ARFI measurements.

Methods: ARFI-induced tissue displacements were simulated with finite-element models(3,4) in a 9 kPa linear elastic solid, using an I_{SPPA}-corrected intensity field modeling a 400 μs ARFI push by a C5-2v Verasonics curvilinear array. The resulting displacement vector field data were used to displace a field of scatterers over a period of 10 ms sampled at 4 kHz. Fullwave(5,6) was used to simulate tracking pulse-echo sequences through the scatterer fields for each time step. Tissue maps of the human abdominal wall were added in the near-field to provide a realistic level of signal attenuation and acoustic clutter. The received channel data were beamformed to produce M-mode data, and LOC was calculated over a 2λ axial region near the focus. Displacements were calculated using Kasai's autocorrelation method(7) with a 2λ smoothing kernel and a bias correction factor, i.e. a ratio between the true and measured displacements, was determined.

Results: Control simulations yielded the highest measured displacement (about 17 μm), and the tissue map simulations yielded lower measured displacements (11-15 μm). A positive correlation between LOC and measured displacement was observed. The bias correction factor monotonically decreased as LOC increased, from a ratio of about 1.8 in the most cluttered environments to about 1 (no correction needed) in zero-clutter environments. Fitting the factor to a linear trend as a function of LOC, we are able to achieve corrected displacement values with less than 5% error from the those of the control case. Future work will involve generalizing these results for a variety of clutter environments.

(1) Kakkad, V et al. *Ultrasonic Imaging, 40* (2018). (2) Long, W et al. *IEEE TUFFC, 65* (2018). (3) Palmeri, M et al. *IEEE TUFFC, 52* (2005). (4) Palmeri, M et al. *IEEE TUFFC, 53* (2006). (5. Pinton, G et al. *IEEE TUFFC, 56* (2009). (6) Pinton, G. *IEEE TUFFC, 64* (2017). (7) Kasai, C et al. *IEEE Tran. Son Ultrason 32* (1985).

8.5 **Efficient calculation of Green's tensor describing shear wave propagation in incompressible, transversely isotropic material**, Ned C. Rouze, Mark L. Palmeri, Kathryn R. Nightingale, *Department of Biomedical Engineering, Duke University, Durham, NC, ned.rouze@duke.edu*

Introduction: Measurements of shear wave propagation following Acoustic Radiation Force Impulse (ARFI) excitation in transversely isotropic materials such as muscle can be analyzed by comparing the observed signals to calculated signals determined using the known excitation geometry and five material constants required to characterize the material. Green's tensor methods provide one method to calculate these signals. However, a closed-form expression for the Green's tensor of a transversely isotropic material is not known, and it is typically calculated using numerical integration techniques. These integrations require large computational effort due to the rapid oscillation of the integrand and thereby limit the utility of Green's tensor calculations for this application.

Methods: By considering an incompressible, transversely isotropic material, the number of constants required to characterize the material is reduced from five to three. In addition, the P-wave propagation mode can be neglected and expressions for the eigenvalues and eigenvectors of the Christofel matrix for the SH and SV propagation modes are simplified. This process allows the Green's tensor to be expressed as the sum of SH and SV contributions with each contribution expressed as the product of multiplicative factors and an integral which is parameterized by three variables. Once these integrals have been precomputed for a range of parameters, the Green's tensor can be evaluated efficiently by combining the multiplicative factors and interpolation within the tabulated integral results.

Results/Conclusions: Evaluation of the Green's tensor was validated by comparing these calculations with known analytic results for the special case of the SH propagation mode. In addition, the results are compared with finite element simulations in an approximately incompressible, transversely isotropic material where the excitation force was applied to a single mesh point to simulate a delta-function excitation. Using the procedure described in this study, the calculation of shear wave signals for a single source point and observation position is sufficiently efficient that Green's tensor methods can be used to calculate shear wave signals for comparison with experimentally observed signals.

9. IMAGING 3

9.1 **Distinguishing solid from fluid breast masses with coherence-based ultrasound imaging**, Alycen Wiacek,[1] Eniola Oluyemi,[2] Kelly Myers,[2] Susan Harvey,[2] Muyinatu A. Lediju Bell,[1,3,4], *[1]Departments of 1Electrical and Computer Engineering, [2]Radiology and Radiological Science, [3]Computer Science, [4]Biomedical Engineering, Johns Hopkins University awiacek1@jhu.edu*

Ultrasound imaging is often used as a supplement to mammography for breast cancer detection. However, false positive rates can be as high as 93% depending on the type of mass in question. Due to the density and heterogeneity of most breast tissue, speed of sound differences can result in the presence of acoustic clutter. This clutter can obscure masses, particularly when deep in tissue, resulting in diagnostic uncertainty, and leading to both false negatives and false positives. By utilizing spatial coherence instead of traditional brightness information,[(1)] this work aims to remove the acoustic clutter that causes diagnostic uncertainty and provide radiologists with an improved ability to distinguish solid from fluid breast masses. Fifteen patients scheduled for biopsy were enrolled in our ongoing study after informed consent and approval from the Johns Hopkins Institutional Review Board. Patients were scanned using an Alpinion ECUBE12R research ultrasound scanner connected to an Alpinion L8-17 linear ultrasound transducer with a transmit frequency of 12.5MHz. The contrast of each mass relative to the background tissue was compared across matched traditional and coherence-based images, created from the same raw data. Due to the spatially correlated content of solid masses when using coherence-based beamforming, solid masses appear to have a similar coherence to that of surrounding tissue with an average contrast of -2.6 dB, appearing significantly different than fluid-filled masses ($p<0.001$), which have an average contrast of -20.7 dB. By displaying coherence information to clinicians in the form of an overlay, we can provide additional insight into the content of breast masses, while retaining the current ultrasound images and standard workflow currently used in the breast imaging clinic.

(1) Wiacek A, et al. *IEEE Trans Ultrason Ferroelect Freq Contr* (2018).

9.2 **Constrained swept synthetic aperture imaging without external tracking**, Nick Bottenus, *Department of Biomedical Engineering, Duke University, Durham, NC, nick.bottenus@duke.edu*

Objective: To demonstrate the application of swept synthetic aperture imaging to extend the effective aperture size without the use of an external tracking device.

Methods: We constrain the tracking problem using a 1-degree-of-freedom circular fixture to move the ultrasound probe, although with unknown temporal dynamics. The ultrasound probe is swept over a phantom or *in vivo* liver target across a 45° arc in under 1 second and image frames are acquired using diverging single-element transmissions to cover a broad field of view. We apply conventional speckle-tracking methods and demonstrate new channel-domain techniques to estimate the motion of the transducer along the prescribed arc. We compare these estimates with the gold standard position measurements made by an external encoder. We use the estimates to reconstruct high-resolution images from the swept synthetic aperture and compare to the images made using the encoder.

Results: The proposed channel-domain estimation technique demonstrates lower estimate jitter than the image-domain speckle correlation techniques. In simulation, lateral translation estimate jitter is reduced from a minimum of 12.3 μm using speckle tracking to 1.3 μm using the channel-domain method. Overlapping estimates from multiple reference frames further reduce both bias and jitter in the estimate. The channel-domain method successfully reproduces both the temporal dynamics of the constrained sweep and, given the prescribed geometry, an accurate magnitude of angular motion. This estimate enables reconstruction of the swept synthetic aperture image without using the external encoder measurement with only minor discrepancies in the resulting high-resolution image.

Conclusion: These results demonstrate that the swept synthetic aperture technique is useful for *in vivo* imaging and that data-based tracking methods can be sufficiently accurate to maintain coherence between probe positions. Supported by NIH grants R01CA211602 from the NCI and R01EB017711 from the NIBIB.

9.3 **Reverberation noise suppression in channel data using 3D fully convolutional neural networks**, Leandra Brickson, Dongwoon Hyun, Jeremy J. Dahl, *Electrical Engineering, Stanford University, Stanford, CA, llbricks@stanford.edu*

Reverberation noise is a result of the ultrasonic wavefront reflecting off multiple surfaces before returning to the transducer. This obscures target anatomy and degrades image quality and diagnosis. Reverberation noise is present in the channel signals, thereby making tasks such as phase aberration correction and adaptive beamforming more difficult. We propose a fully convolutional neural network with a custom architecture to eliminate clutter from ultrasound channel signals.

A simulated dataset of full synthetic aperture channel signals was generated in Field II Pro on the Verasonics L12-3v transducer to train the network. Reverberation noise was included by adding bandpass-filtered random noise to the simulated channel data. Thermal noise (white noise) between -20 and 10 dB was also added. Channel-signal-pairs before and after adding noise were used as the training set to train a fully convolutional neural network to remove the thermal and reverberation noise, using the L2 norm as the network loss function. The trained network was evaluated on a simulated test set, similar to the training set, with -10 to 20 dB added reverberation noise. The network was also tested on an ATS 549 phantom using an L12-3v transducer connected to a Verasonics Vantage 256 system. Fatty bovine tissue was inserted between the transducer and phantom to create reverberation noise.

The resulting network significantly reduced reverberation and thermal noise in the output channel signals. The RMS error improved from 1.37 between the noisy data and the noise-free data, to 0.97 between the noise free data and the network output. The lag one coherence improved from 0.50 in the noisy data to 0.99 after passing through the neural network. Significant smoothing across the channels is also clearly visible. In the phantom data, anechoic lesion contrast improved from -14.0 to -29.9 dB.

9.4 **Phase aberration correction by time-delay computation from local sound speed estimation**, Rehman Ali, Jeremy J. Dahl, *Stanford University, Department of Radiology, jeremy.dahl@stanford.edu*

Phase aberration has long been identified as major sources of image degradation in medical ultrasound; however, existing near-field and distributed aberration correction techniques have shown limited ability in improving image quality. We propose a distributed phase aberration correction technique that is practicable to implement and significantly improves image quality.

In this method, the local sound speed (*c*) in the medium is estimated by solving a model that relates measurements of the global average sound speed at every point in the medium to the local sound speed. The eikonal equation is then used to solve for the travel times between each array element and every point in the image, using the local sound speed estimates. The resulting propagation delays were subsequently applied to multistatic synthetic aperture data to obtain aberration-corrected images. Fullwave simulations in two-layer media were performed to validate the method (*c* in top layer = 1480 m/s, *c* in bottom layer = 1600 m/s). Experiments in tissue-mimicking phantoms with an L12-3v array and Vantage 256 scanner included a layer of graphite slurry (*c* = 1540 m/s) or porcine tissue (unknown *c*) placed on top of an ATS Model 549 phantom (*c* = 1460 m/s).

Point target resolution in the simulations decreased by 102% with conventional beamforming and 45% using near-field phase correction, relative to a homogeneous medium. In the proposed method, resolution was completely restored. Target position error was 0.41, 0.38, and 0.07 mm laterally, and 0.57, 0.44, and 0.01 mm axially, for the three beamforming methods, respectively. In the phantom experiments, the proposed method produced significantly improved image quality, including a 62% improvement in resolution and improved target contrast, compared to beamforming using a constant sound speed.

9.5 **Multi-covariate imaging of sub-resolution targets: initial clinical results**, Matthew Morgan[1], Gregg Trahey[1,2], William Walker[1,3], *Departments of [1]Biomedical Engineering, [2]Radiology and [3]Electrical Engineering, Duke University, Durham, NC, mrm63@duke.edu*

Objectives: The conventional approach to ultrasound beamforming relies on a simple delay-and-sum model. Many alternative beamforming methods have been proposed to improve image quality by using aperture domain spatial coherence as a contrast mechanism. However, these methods are limited by the use of simplistic models of signal coherence, and *ad hoc* methods of extracting information. We have developed a novel imaging method, Multi-covariate Imaging of Sub-resolution Targets (MIST), which assumes clinical targets consist of diffuse, unresolvable targets, whose statistical properties can be imaged directly. The goal of this work is to evaluate the performance of MIST in fetal and liver imaging environments.

Methods: Echo data of fetal and liver targets were collected from a number of patients at the Duke University Medical Center under IRB-approved protocols. Fundamental and harmonic channel data were collected using a Verasonics Vantage research scanner and a C5-2v curvilinear array. Conventional B-Mode and MIST images were formed and evaluated using contrast, contrast-to-noise ratio (CNR) and speckle signal-to-noise ratio (SNR).

Results: MIST demonstrated quantitative and qualitative improvements in image quality over conventional B-Mode. Liver and fetal images demonstrated improved contrast, CNR, and speckle SNR for MIST relative to B-Mode. Speckle texture was noticeably smoothed, with improved border delineation and conspicuity of hypoechoic targets, without a loss in lateral resolution. MIST was shown to preserve native target contrast and to be temporally-stable in the presence of noise.

Conclusions: These results suggest MIST is a clinically-viable image formation method capable of improving image quality across a range of clinical targets.

Friday morning

10. TISSUE PARAMETERS 2

10.1 **Modeling ultrasound attenuation in random porous structures mimicking cortical bone, using Independent Scattering Approximation (ISA): Solving the direct and inverse problems**, Omid Yousefian[1], R.D. White[2], H.T. Banks[2], Marie Muller[1], [1]*Mechanical and Aerospace Engineering Department*, [2]*Center for Research in Scientific Computation, NC State University, Raleigh, NC 27695-8212, oyousef@ncsu.edu*

The goal of this study is to estimate the porosity (pore size and density) of numerically simulated random porous 3D structures mimicking simplified geometries of cortical bone using attenuation of ultrasonic waves in MHz range. To do so, we use a physics-based model derived from the independent scattering approximation to model the frequency-dependent attenuation of elastic waves in porous structures as a function of the parameters we wish to identify, pore size and density. Frequency-dependent attenuation data is generated using 3D finite-difference time-domain simulations in the range of 1-8 MHz in mono-disperse structures with pore diameter and density ranging from 100-200 μm and 20-50 pore/mm^3, respectively. We then solve the inverse problem using an ordinary least squares (OLS) method to recover the porosity parameters, by minimizing the sum of squared errors between the simulated data and the model prediction. In doing so, we verify that we can estimate with confidence the parameters quantifying porosity using a model based on the Independent Scattering Approximation, on 3D numerically-simulated attenuation data.

10.2 **Effects of microstructure on attenuation, scattering and apparent absorption coefficients: Application to porous structures mimicking cortical bone**, Yasamin Karbalaeisadegh, Omid Yousefian, Marie Muller, *Department of Mechanical and Aerospace Engineering, North Carolina State University, Raleigh, NC, mmuller2@ncsu.edu*

Wave propagation in biphasic porous structures is associated with losses due to scattering as a result of acoustic impedance differences between the components and absorption losses within the medium. Size and distribution of the components, as well as the operating frequency, affect the total attenuation. 2D finite-difference time-domain simulations are run to model the propagation of 8 MHz plane waves in porous structures mimicking cortical bone. Material properties of cortical bone and water are respectively assigned to the solid and liquid phases of the monodisperse structures with different pore diameters ($\phi \in [40 - 120]$ μm) and pore densities ($n \in$ [5-25] pore/mm^2). The attenuation coefficient of each structure is measured by fitting the exponential decay of the received signal amplitude both for absorbing (coefficient of dB/(10 cm.Mhz) to mimic bone tissue) and non-absorbing cases. The latter gives the attenuation exclusively due to scattering (α_{scat}) and by subtracting α_{scat} from the total attenuation, apparent absorption coefficient ($\alpha_{app.abs.}$) is obtained which represents the absorption losses in the medium. For highly scattering regimes ($k\phi>1$; k: wavelength), an increase in either pore size or density results in an increase in $\alpha_{app.abs}$ while α_{scat} remains constant. This is counter-intuitive since one would expect than a smaller portion of absorbing tissue would lead to a small overall absorption. We hypothesize that the presence of multiple scattering in the medium leads to longer paths in the absorbing solid phase, leading to a higher apparent absorption coefficient. On the other hand, in low/intermediate scattering regimes where $k\phi<1$, an increase in either ϕ or n results in an increase in α_{scat} while $\alpha_{app.abs}$ remains constant and equal to the input absorption coefficient value for simulations dB/(10 cm.Mhz)).

10.3 **Extraction of micro-architectural properties of cortical bone using ultrasound attenuation and an artificial neural network**, Kaustav Mohanty, Omid Yousefian, Yasamin Karbalaeisadegh, Micah Ulrich, Marie Muller[1], [1]*Department of Mechanical and Aerospace Engineering, NC State University, Raleigh, NC-27695, kmohant@ncsu.edu, mmuller2@ncsu.edu*

This study aims at estimating micro-architectural properties of cortical bone such as pore diameter, pore density and porosity from ultrasound attenuation measurements using an artificial neural network (ANN). 2D finite-difference time-domain simulations are conducted to calculate the frequency-dependent attenuation in the range of 1-8 MHz in mono-disperse structures (constant pore size) with pore diameter and density ranging from 20-120 microns and 3-16 pore/mm^2 respectively. Furthermore, poly-disperse structures (non-uniform pore distribution) are obtained from high resolution CT scans of human cortical bone and 2D numerical simulations of ultrasound propagation are carried out in the same frequency range. Using image processing, the distribution of pore diameter, porosity and pore density are calculated. This data is used for the training data set. The dataset consists of 330 structures for the mono-disperse model and 640 structures for the poly-disperse model.

An ANN was developed using Python (Keras), with 3 hidden layers and 615 trainable weights. The frequency-dependent attenuation was utilized as the feature vectors. The desired outputs were set as the micro-architectural properties, namely the average pore diameter, pore density and porosity. The ANN was found to have an accuracy of 88% and loss of 2.64%. The R-squared values between the actual parameters and predicted parameters were found to be 0.84 (slope = 0.91), 0.95 (slope = 0.96), 0.96 (slope=0.96) and 0.97 (slope 0.96) for pore density, average pore diameter, standard deviation of pore diameter and porosity respectively. This work demonstrates the potential of combining ultrasound methods with deep neural networks to quantify cortical bone parameters with high accuracy.

10.4 **Detection and staging of Idiopathic Pulmonary Fibrosis (IPF) using ultrasound backscattering and diffusivity: *In vivo* rodent study**, Kaustav Mohanty[1], John Blackwell[2], Mir Ali[2], Thomas Egan[2], Marie Muller[1], [1]*Department of Mechanical and Aerospace Engineering, NC State University, Raleigh, NC-27695,* [2]*Division of Cardiothoracic Surgery, Dept. of Surgery, UNC Chapel Hill, Chapel Hill, NC-27599,* kmohant@ncsu.edu

Idiopathic pulmonary fibrosis (IPF) is a disease responsible for changes in the micro-architecture of the parenchyma, such as thickening of the alveolar walls, which reduces compliance and elasticity and affects the porosity. In this *in-vivo* study, we verify the hypothesis that changes in the micro-architecture of the lung parenchyma can be quantified by measuring the diffusivity of the backscattered ultrasonic waves. In highly complex media such as the lung parenchyma, traditional ultrasound imaging fails due to multiple scattering. We take advantage of the fact that ultrasound propagation in a highly scattering regime is diffusive in nature and can be characterized using the Diffusion Constant. We hypothesize that in a fibrotic lung, the thickening of the alveolar wall reduces the portion of air-filled alveoli, thereby reducing the scattering events.

Pulmonary fibrosis is created in Sprague-Dawley rats by instilling bleomycin into the airway. The rats are studied in groups of n=6 (3 male and 3 female) 2, 3, and 4 weeks after bleomycin administration, corresponding to various degrees of severity of pulmonary fibrosis. Using a 128-element linear array transducer operating at 7.8MHz, the Diffusion Constant is measured *in-vivo* via the quantification of the rate of growth of the diffusive halo. The rats are then euthanized and Computed Tomography scans are performed to quantify the degree of fibrosis created. Significant differences ($p<0.05$) in the D values between control and fibrotic rats showcase the potential of this method for diagnosis and monitoring of IPF.

11. TISSUE PARAMETERS 3

11.1 **Breast tumor classification using homodyned K distribution**, Ehsan Ul Islam Abir[1], Goutam Ghoshal[2], Sabiq Muhtadi[1], Shaiban Ahmed[1], Rasheed Abid[3], Juan Shan[4], S.N. Akhlaghi[5], Brian S. Garra[5], Rafiul Hasan[6], S. Kaisar Alam[7,8,9], [1]*Islamic University of Technology, Gazipur, Bangladesh,* [2]*AIDI Engineering, South Grafton, MA,* [3]*Uttara University, Dhaka, Bangladesh,* [4]*Pace University, New York, NY,* [5]*Food and Drug Administration, Silver Spring, MD,* [6]*King Fahd University of Petroleum and Minerals,* [7]*Imagine Consulting Services, Dayton, NJ,* [8]*CBIM, Rutgers University, Piscataway, NJ,* [9]*The College of New Jersey, Ewing, NJ, Nima.Akhlaghi@fda.hhs.gov*

Objectives: Our aim is breast mass classification of ultrasound grayscale images using parameters of the homodyned K distribution of the envelope of the backscattered echo. Our results suggest that the homodyned K distribution can effectively classify benign and malignant breast masses and the performance is better for masses that are clearly visible.

Methods: Radiofrequency (RF) breast ultrasound data from 136 patients were acquired (101 benign masses and 35 malignant masses, as indicated by biopsy). We subclassified these patients into Clearly Visible Mass (CVM) and Not Clearly Visible Mass (NCVM). Of the 35 malignant masses, 18 were CVM and 17 were NCVM. Of the 101 benign masses, 57 were CVM and 44 were NCVM. Parameters of homodyned K distribution, μ (number of scatterers per resolution cell) and k (periodicity in scatterer locations) were calculated for each mass. Linear Discriminant Analysis (LDA) was performed with μ against k and the classification performance was estimated using 5-fold cross-validation.

Results: LDA was performed twice, one for CVM (LDA1) and the other for the whole data set (LDA2). LDA1 showed a classification accuracy of 88% with area under ROC curve (AUC) of 0.85. The number of true positives was 12 out of 18 malignant CVMs and the number of true negatives was 54 out of 57 benign CVMs. LDA2 showed a classification accuracy of 76% with an AUC of 0.81. The number of true positives was 14 out of 35 malignant masses and the number of true negatives was 90 out of 101 benign masses.

Conclusion: Parameters of the homodyned K distribution performed well in classifying benign and malignant masses. However, CVM showed better classification than NCVM. Thus, lesion visibility affects lesion classification using the homodyned K distribution.

11.2 **New way to detect fiber-like structures using effective scatterer diameter estimation**, Mohammadreza Kari[1], Helen Feltovich[1,2], Timothy J. Hall[1], [1]*Medical Physics, University of Wisconsin - Madison, Madison, WI,* [2]*Maternal Fetal Medicine, Intermountain Healthcare, Provo, UT,* *mkari@wisc.edu*

Objectives: Some tissues (e.g., skeletal muscle, tendon, renal cortex) exhibit backscatter anisotropy because of elongated structure. We previously reported the use of electronically-steered beams to detect anisotropic backscatter. This new technique provides an alternative approach and also proposes a way to improve effective scatterer diameter (ESD) estimation in such media.

Methods: The frequency dependence of scattering from a collection of cylindrical scatterers in the Rayleigh scattering condition is proportional to the frequency-cubed. Therefore, for a medium with unknown scattering sources, the experimental form factors are obtained by dividing the measured backscattering coefficients by frequency-cubed (new definition) and also by the fourth power of frequency (common definition). In the next step, the model (e.g., Gaussian) form factor is fit to both measured form factors and the Chi-square parameter (χ) is computed for each fit. The fit with minimum (χ) indicates the most likely type of scattering source.

Results: The new technique was applied on form factor data from a phantom with random fibers (of 130 μm diameter) and on the bicep muscle. For both cases, the Gaussian form factor model fit very well on the measured form factor using the newly defined form factor. The ESD of the phantom using the new form factor definition of was estimated as 204 μm while it was computed as 315 μm using the common definition of form factor. In the case of bicep muscle, the average Chi-square values, 0.0055 and as 0.0084 with the new and common form factor definitions, respectively, indicating the presence of fiber-like structures in this tissue.

Conclusions: The proposed technique is able to detect the presence of elongated structures in phantoms and soft tissues that contain fiber-like scatterers. It suggests the potential of this technique for objective quantification of the presence of fiber-like structures in complex biological tissues without the need for beamsteering data. We are grateful to Siemens Ultrasound for an equipment loan and technical support. This research was supported by NIH Grant R01HD072077. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

11.3 **Ultrasound thermometry for HIFU therapy: CNN LSTM approach,** Changfan Chen[3], Younsu Kim[1], Chloe Audigier[3], Ari Partanen[4], Emad Boctor[1,2], [1]*Department of Computer Science,* [2]*Department of Radiology,* [3]*Laboratory of Computational Sensing and Robotics, Johns Hopkins University, Baltimore, MD,* [4]*Profound Medical Corp, Mississauga, Canada, eboctor1@jhmi.edu*

Introduction: HIFU (High intensity focused ultrasound) uses of focused ultrasound wave on a target to increase temperature and is widely used due to its noninvasiveness and quick recovery after an ablation procedure. Our goal is to monitor temperature change in the body accurately using ultrasound during HIFU procedure. Temperature monitoring is essential for preserving surrounding healthy tissues while destroying target tissues. MRI images are used to monitor the temperature; however, MRI is too expensive and not portable while ultrasound system is cheap and portable.

Method: Our 256 elements HIFU system alternates monitoring phases and ablation phases. An ultrasound probe with 128 elements is placed on top of body to receive signals. Channel data is collected from the ultrasound probe to generate a temperature image and determine whether the cell is still alive or not. Using the information from monitoring phases, we design a deep learning network to convert from channel data to temperature images. We obtain MRI temperature images simultaneously as a ground truth to train the network. We conducted phantom experiments to collect data for 5 monitoring phases.

Results: Comparison between MRI temperature images and ultrasound temperature images was made to evaluate the reconstruction accuracy. We calculated pixelwise mean and max error in each image. The error was in a small range, which shows the feasibility of the technology.

Conclusion: We showed that temperature images can be generated from ultrasound channel data with a deep learning method. Future studies will mainly focus on *in vivo* experiments and more generalized models with different tissues.

11.4 **Comparison of deep-learning and classical image processing for skin segmentation**, Felix Jin[1], Michael Postiglione[1], Anna Knight[1], Adela R. Cardones[2], Mark Palmeri[1], [1]*Department of Biomedical Engineering, Duke University, Durham, NC,* [2]*Department of Dermatology, Duke University Medical Center, Durham, NC, fqj@duke.edu*

Accurate determination of skin thickness from ultrasound images is necessary for a variety of applications, such as tracking disease progression, guiding procedures, and measuring certain tissue properties. In particular, our lab uses shear wave elasticity imaging to measure skin stiffness, which requires accurate skin (dermis) segmentation on B-mode images. In this work, we applied classical image processing and deep-learning methods to skin segmentation and compared their performances.

Previous literature on automatic skin segmentation has relied on image differentiation for edge detection. In addition, we also evaluated Otsu's thresholding. For deep learning, we designed and trained a convolutional neural network to take B-mode images and output central skin thickness. Our training dataset consisted of 538 unlabeled skin B-mode images acquired using a Siemens Acuson SC2000 scanner with a VF14-5 linear array operating at 8 MHz across a variety of anatomic locations. Images were reconstructed from harmonic IQ data with no additional processing. These images spanned 38 mm laterally and 16 mm in depth. Ground truths for training the deep-learning model were generated from manually-inspected segmentations produced by Otsu's method. A set of 213 images from a different study were used for testing the final performance of each method. All predicted segmentations were evaluated manually under randomized and blinded conditions.

Image differentiation performed well for the proximal skin edge but failed to find the distal edge due to relatively poor edge contrast with the subcutaneous tissues. Otsu's method performed the best, accurately segmenting 55.2% and 43.7% of the training and test datasets respectively. The deep-learning model correctly segmented 55.4% of the training and 39.4% of the test images. Our results show that deep-leaning methods can perform similar to classical image processing methods but may become less robust when applied to different data.