UITC Abstracts 2023

Monday Morning June 5th
1. Speed of Sound & Shear Wave Elasticity Session

1.1. Global Average Sound Speed Estimation Through a Tissue Mimicking Aberrating Layer. Thurston Brevett, Sergio Sanabria , Arsenii Telichko, Jeremy Dahl, *Stanford University, Department of Radiology, Stanford, California USA, tbrevett@stanford.edu*

Background: Quantitative estimation of the global average sound speed is a promising capability for pulse-echo ultrasound systems as knowledge of the sound speed can be used for quantitative diagnostics as well as for aberration correction. Prior work has linked the sound speed in tissue to its disease state. Other preliminary work has shown that the sound speed can be used for aberration correction. Recently, we have developed a technique to estimate the global average sound speed from full synthetic aperture data.

Methods: Our method operates by first selecting a sub-aperture, applying a move-out operation using an a-priori sound speed, and then applying a spatio-temporal filter. With the filtered data, we then estimate the time-of-flight to a scatterer location and estimate the sound speed from the time-of-flight using a regression technique. In this work, we have expanded our approach to include off-axis scattering and larger sub-apertures. We tested our estimator on simulations of a multi-layered speckle generating medium and real data acquired from a tissue-mimicking aberrating layer of chicken breast and an agar-propanol speckle-generating phantom with a Verasonics L12-3v probe.

Results: In simulations of multi-layered media, we achieve estimates of the sound speed within as low as +/- 2.5 m/s root-mean-square error (RMSE) for layered media with a bias of about -2 m/s. In real data, our estimates gradually decrease from 1630 m/s to 1540 m/s, consistent with a sound speed of 1590 m/s within the aberrating layer and 1490 m/s within our phantom. We discuss appropriate selection of parameters that affect accuracy, such as the spatial-temporal filter cutoff, the off-axis scattering angle, and the aperture size.

Conclusions: We have shown accurate estimates for axial and non-axial scattering in layered media models. Furthermore, we demonstrated the efficacy of our method with real data. These advances provide a basis to compute the local sound speed via an inversion method. We preview preliminary results suggesting that these estimates are sufficient to provide a significant improvement in image resolution.

1.2. Local reconstruction of speed-of-sound in a murine model of nonalcoholic fatty liver with spatiotemporal filtering of full-synthetic aperture data. Sergio Sanabriaa[b], Thurston Brevett[a], Arsenii Telichko[a], Jeremy Dahl[a], *[a]Stanford University, Department of Radiology, Stanford, California USA, [b]Deusto Institute of Technology, University of Deusto/ IKERBASQUE, Basque Foundation for Science, Bilbao, Spain. sanse@stanford.edu*

Background: Speed-of-sound (SoS) in the liver has been postulated as a quantitative biomarker for stratification of non-alcoholic fatty liver disease (NAFLD). SoS in adipose tissue is lower than in healthy liver. Recently, we have proposed a pulse-echo SoS reconstruction method based on full synthetic aperture (FSA) data. While existing methods apply a delay-and-sum or similar beamforming operation, in our method we apply delays and a spatio-temporal filter and then correlate channels directly without summing, thus avoiding spatial biases when the sound speed is mismatched. Here we analyze the feasibility of this method to reconstruct SoS in murine liver.

Methods: We reconstructed local SoS in 4 lean Zucker rats fed a normal diet and 16 obese rats fed a high fat diet for up to 8 weeks. Local SoS was reconstructed in 4 steps: non-axial scattering contributions were filtered out from FSA; time-shifts were measured within different mid-poing gather subaperture; average scatterer depth was estimated for each aperture; and tomographic reconstruction of local SoS was performed. In-vivo estimation was performed for 8 rats, and the remaining 12 were measured post-mortem. The SoS ground truth was obtained from the excised liver with an established calibration setup.

Results: The high respiration rate (2-3 breaths per data acquisition) impacted local SoS reconstruction. For post-mortem measurements, SoS ranged 1530-1570 m/s. SoS was reconstructed with a rmse of 12 m/s with respect to ground truth. The average std. deviation of SoS within murine liver was 6 m/s. SoS correlation with adipose fraction was R2 = 0.44. SoS measurements were well-correlated with local SoS calculated from coherence-based average speed-of-sound estimates obtained with beamforming (R2 = 0.96).

Conclusions: Local SoS estimation in murine models is feasible in murine models, with correlations with adipose fat fraction content. Results are consistent with both previous local SoS methods based on beamforming and with ground truth measurements.

1.3. Estimation of Abdominal Sound Speed Distributions using Neural Networks Trained on Wave Propagation Physics in the Human Body. Louise Zhuang[1], Walter Simson[1], Oleksii Ostras[2], Dongwoon Hyun[1], Gianmarco Pinton[2], Jeremy Dahl[1], *[1]Stanford University, Stanford, CA, USA, [2]Joint Department of Biomedical Engineering at the University of North Carolina at Chapel Hill, and North Carolina State University, Chapel Hill, NC, USA. llz@stanford.edu*

Background and Objective: Aberration correction and estimation has persistently challenged ultrasound imaging and remains critical for improving image quality at depth and in patients with large body habitus. Hepatocellular carcinoma, for example, often has degraded image quality that impairs clinical diagnosis because fat, muscle, and connective tissue layers induce substantially different aberration than homogeneous assumptions. The most sophisticated aberration correction approach involves determining the tissue sound speed distribution and calculating spatially varying beamforming delays using that distribution. Here, we approach sound speed estimation from a physics and algorithmic perspective. We develop a neural network that predicts sound speed maps generated from an in-silico liver imaging dataset using anatomically derived human body wall maps and propagation physics simulated by Fullwave 2.

Methods: We created a dataset of simulated RF data from a C5-2V transducer using a full synthetic aperture pulse sequence. Two-dimensional simulation fields of the human abdominal wall and liver were obtained from segmented volumes from the Visible Human Project, and acoustical properties used in each simulation were sampled from the distributions of values for each tissue. We then trained a neural network through supervised learning to predict sound speed maps corresponding to pixel locations of input beamformed IQ data from the simulations. During training, 25% of samples were augmented with thermal noise for increased robustness.

Results and Discussion: The neural network reasonably predicted sound speed distributions containing clear tissue structures, even with varying amounts of thermal noise. On a test set, the predicted sound speed maps had an average RMSE of 42.8 m/s and MAE of 27.6 m/s. We examine this network on its ability to adapt to real scanner data using a CIRS phantom with an aberrating layer. These results show potential for using neural networks for sound speed estimation in abdominal ultrasound scans, which could lead to improved diagnosis and treatment of liver cancer.

1.4. Advanced multi-lag approaches for improving shear wave elastography applications. E. G. Sunethra Dayavansha[1], Ali Kafaei Zad Tehrani[1], Yuyang Gu[1], Marko Jakovljevic[1], Kai Thomenius[1], Mike Wang[2], Rimon Tadross[2], Anthony E. Samir[1], *[1]MGH and HMS, [2]GE Healthcare, sdayavansha@mgh.harvard.edu*

Shear wave speed (SWS) estimation with increased confidence is vital in diagnostic applications of shear wave elastography (SWE). Usually, SWS values are computed by using the time delay estimates in the displacement profiles of the medium considering a pair of spatial locations with a known spatial lag (offset) from each other. Significant dependence of SWS estimation accuracy on spatial lag value indicates the need for optimized techniques utilizing multiple lags (combination of locations) in reconstructing SWS. Utilizing multi-lag approaches, the robustness to errors or noise, spatial resolution and temporal stability can be improved.

Previously, model-based multi-lag approaches were applied in simulated SWE data to illustrate possible enhancement to contrast-to-noise ratio and spatial resolution. In this work, the feasibility to adapt model-based multi-lag approaches with pre-defined lag ranges and kernels is demonstrated using phantom and in vivo data. Additionally, the opportunity for further improvements by incorporating quality metrics in the multi-lag framework is illustrated. The improvements in shear-wave images are quantified using the bias and variance comparisons between single-lag and advanced multi-lag approaches. In phantom acquisitions, the multiresolution approach can reduce the variance by up to 80% and bias by up to 60% relative to the corresponding single-lag based shear-wave images. For in vivo acquisitions, we explore the potential of the multi-lag approach to 1) reduce the required number of tracking and push pulses while maintaining image SNR and quality of shear wave estimates comparable to those of the fully sampled acquisitions and 2) reducing variability of SWE estimates between multiple frames.

1.5. Shear Modulus and Viscosity Changes in the Pancreatic Tumor Microenvironment in Response to Stereotactic Body Radiation and Immunotherapy. Nikhila Nyayapathi[1], Tara Vrooman[2], Angela Hughson[2], Scott Gerber[2], Marvin Doyley[1], *[1]Department of Electrical and Computer Engineering, University of Rochester, [2]Department of Microbiology and Immunology, University of Rochester Medical Center, m.doyley@rochester.edu*

Pancreatic ductal adenocarcinoma is a lethal disease with very high mortality rates. It is also asymptomatic until advanced stages, which is why only about 20% of patients are eligible for curative resection. Neoadjuvant therapies aim to downgrade tumors for patients with borderline resectable masses. In this work, we study changes in shear modulus, viscosity, and vascularity in the tumor microenvironment for various treatment groups. Four treatment groups were used – (1) untreated or control, (2) Stereotactic body radiation (SBRT) only, (3) IL-12 only, and (4) SBRT + IL-12.

40 female mice were injected with KP2-1 (Luc/RFP) 2.5 x 104 cells were injected on Day 0. Two 4 mm titanium fiducial clips were surgically implanted for SBRT. SBRT (6 Gy) was performed from Day 6 to 9 using a small animal radiation research platform (SARRP). On Day 10, 0.5 □g in 25 □l volume of sc-mRNA or IL-12mRNA were injected into the tumor. Plane-wave single-track location shear wave elasticity imaging (pSTL-SWEI) was performed in vivo using a 128-element linear array transducer (L11-5v, Verasonics, Inc.). Animals were anesthetized with 3% isoflurane and their abdominal region was shaved. The tumor region was identified using B-mode, and SWEI was acquired at three transverse cross sections of tumor. Average shear wave speed and viscosity was calculated over all three cross sections. Mice were imaged over 42 days at 8 time points (Days 14, 16, 20, 23, 27, 30, 34, and 42).

Shear wave speeds for untreated group was the highest, followed by SBRT, IL-12 and SBRT+IL-12 groups respectively. We found that the viscosity trend was reversed. These results indicate that shear wave speed and viscosity could be used to reliably differentiate between various treatment groups. We are currently studying the histopathology of tumors as well as their vascular characteristics.

1.6. Robot-Assisted 3D Rotational Shear Wave Elasticity Imaging. Shruthi Srinivasan, Courtney Trutna-Paley, Wren Wightman, Kathryn R. Nightingale*, Duke University*

We have previously developed rotational 3D SWEI as a robust method for observing 3D shear wave propagation in soft tissue from a central push beam. In this talk, we will discuss the design and implementation of a novel robot-assisted rotational SWEI ultrasound system. This system builds on existing methods for rotational SWEI [1] and robot-assisted ultrasound imaging techniques [2], with the ability to rotate at a constant speed while obtaining SWEI imaging data and concurrently monitoring force-feedback. This is accomplished with the implementation of a Universal Robot UR10e (CIMTEC Automation). This co-bot allows for assisted manual guidance of the ultrasonic transducer to the proper acoustic window, then locking and rotating about a central axis at a specified angular speed. Our system first accelerates the rotation to a constant speed and then obtains sequentially triggered planar SWE data while rotating. An inherent tradeoff exists between faster rotational speeds and motion artifacts arising from rotating while imaging. We balance this by harnessing the advantage of much more rapid SWEI volume data acquisition in the clinic using the co-bot, which translates to more measurements during the exam period, decreased likelihood of patient motion impacting data acquisition, and the ability to obtain data during active muscle contraction. As such, in this study we propose to investigate the impact of rotational speed on the accuracy, bias, and precision of 3D-SWE measurements in order to determine the optimal rotational speed and triggering sequences for our upcoming clinical studies.

Previous studies have achieved a rotational speed of 20 degrees/second, with .036 s of tracking information after each push [1]. Herein we investigate speeds of up to 100 degrees/second in calibrated homogenous viscoelastic phantoms. Additionally, we will evaluate system performance using varying rotational speeds in ex-vivo muscle and in-vivo human skeletal muscle to validate preliminary results. Alongside rotational speed analysis, methods for compressional force monitoring will also be integrated using the co-bot's built-in force sensor to monitor normal force on the medium during imaging.

[1] Knight AE, Trutna CA, Rouze NC, Hobson-Webb LD, Caenen A, Jin FQ, Palmeri ML, Nightingale KR. Full Characterization of in vivo Muscle as an Elastic, Incompressible, Transversely Isotropic Material Using Ultrasonic Rotational 3D Shear Wave Elasticity Imaging. IEEE Trans Med Imaging. 2022 Jan;41(1):133-144. doi: 10.1109/TMI.2021.3106278. Epub 2021 Dec 30. PMID: 34415833; PMCID: PMC8754054.

[2] G. Ma, S. R. Oca, Y. Zhu, P. J. Codd and D. M. Buckland, "A Novel Robotic System for Ultrasound-guided Peripheral Vascular Localization," 2021 IEEE International Conference on Robotics and Automation (ICRA), Xi'an, China, 2021, pp. 12321-12327, doi: 10.1109/ICRA48506.2021.9561924.

1.7. Ultrasound Imaging Biomarkers for Myofascial Pain Syndrome. Cristian Rios[1], Matin Jahani Jirsaraei[1,2], Siddhartha Sikdar[1,3], *[1] Department of Bioengineering, George Mason University, Fairfax, VA. [2] Department of Civil Engineering, George Mason University, Fairfax, VA, [3] Center for Adaptive Systems of Brain-Body Interactions, George Mason University, Fairfax, VA*

Background: Myofascial pain syndrome (MPS) is a highly prevalent cause of chronic musculoskeletal pain. It is estimated to be prevalent in 30% to 85% of pain patients. The current diagnostic criteria for MPS is through physical examination. A key characteristic of MPS, recognized by many but not all clinicians, is the presence of myofascial trigger points (MTrPs), that are palpable tender nodules that may be spontaneously painful (active), or painful on palpation (latent). However, physical evaluation of MPS has been noted to be unreliable. The lack of training and/or experience with MTrPs limits proper diagnosis and thus appropriate treatment of MPS. There is an unmet need for objective biomarkers to characterize, quantify, and monitor MPS and its response to treatment. This need for appropriate diagnosis and management of chronic pain that does not rely on opioids is especially urgent in view of the ongoing opioid epidemic.

While the pathophysiology of MPS is still not well understood, there is emerging evidence on the role of biomechanics of fascia. Fascia consist of a continuous hierarchical network of connective tissue linking individual muscle fibers to the tendons and bone, and abnormalities in its gliding (shear) mechanics have been implicated in the development of MPS. This impacts the viscoelastic properties and mechanical mobility of muscle tissue. Diagnostic ultrasound (US) has shown merit over recent years for characterizing and evaluating MPS. Ultrasound shear wave elastography (SWE) is an attractive modality to quantify the shear mobility of muscle tissue. Our research study aims to develop quantitative biomarkers informed by the current understanding of underlying tissue-level mechanisms at the level of the "myofascial unit" (muscle, nerve, fascia, vasculature, lymphatics) that are likely to be involved in MPS.

Methods: In this study, we investigated the reproducibility of handheld SWE, for characterizing muscle tissue and how it can be applied to evaluate shear anisotropy trends in different population groups with active, latent, and normal TrPs. The reproducibility of manual SWE was completed by evaluating a total of twelve healthy patients among three different devices (Siemens, Cannon, Samsung) at a similar muscle tissue position. Furthermore, shear anisotropy of active, latent, and normal TrPts was characterized using Aixplorer Supersonic SWE manually at 10-degree intervals between -90□ to 90□ in the upper trapezius muscle. This initial two-phase study provided preliminary data on how SWE data acquisition methodology can be optimized and potential biomarkers for TrPs can be extracted from SWE data.

Results: In a preliminary study of 15 subjects, we observed a statistical difference in shear anisotropy among active and latent TrPs, and normal muscle– showing merit of shear anisotropy being a potential biomarker. However, in comparing shear wave speed at the same muscle tissue position within the same and between different device manufactures using handheld SWE in 12 healthy subjects at six locations on the lower leg, we observed a high coefficient of variation (17-23%). Some potential sources of variability include placement of transducer, applied pressure, stabilization period, operator variability, and methods of estimating shear speed. This variability impacts the ability to develop a biomarker with SWE, and in ongoing studies we are investigating a more automated methodology to estimate shear anisotropy to tackle current limitations. Lastly, ongoing studies are currently evaluating additional ultrasound modes, including B-mode and color doppler, as additional imaging methods to extract additional qualitative and quantitative biomarkers for further characterizing the myofascial unit.

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Monday Afternoon June 5th
2. Quantitative Ultrasound Session

2.1. Addressing the Effect of Chest Wall Thickness in Lung Tissue Characterization. Azadeh D. Cole, Marie Muller, *University of North Carolina*

Ultrasound imaging, in contrast with other imaging modalities (CT, X-ray, and MRI), has recently emerged as a safe, non-radiative, and portable solution for lung imaging. However, conventional pulse-echo ultrasound imaging is very challenging in air-filled porous media such as the lung or bone due to multiple scattering by the complex tissue microstructure. The coherent wave is challenging to track as it propagates through the highly scattering lung tissue. While conventional ultrasound imaging fails to render a clear image of lung structure, useful information pertaining to the microstructure can be extracted through the statistical analysis of their acoustic properties. We developed quantitative ultrasound-based methods to describe micro-structural changes in the lung parenchyma associated with lung diseases. Ultrasound raw data acquisition is affected by the presence of ribs and the chest wall thickness. To avoid the backscattered signals from the ribs, the ultrasound probe is placed in the intercostal space, between the ribs for data acquisition. To minimize the effects from the chest wall thickness (the distance between the skin surface and the lung surface) we suggest

and explore advanced data acquisition methods such as Gaussian Beamforming. We hypothesize that by forming an array of virtual point-like sources on the lung surface, we will minimize the effect of the chest wall thickness and acquire more robust backscattered signals from the lung medium.

2.2. Ultrasound Imaging of Muscle Function During Dynamic Physical Activity. Erica L. King[1,2], Ahmed Bashatah[1], Brian M. Guthrie[3,4], Margaret T. Jones[3,4,5], Qi Wei[1], Siddhartha Sikdar[1,2], Parag V. Chitnis[1,2],
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Introduction: Current musculoskeletal ultrasound (MSK-US) requires operator-dependent examinations which is suboptimal when examining muscle function during dynamic movement. We have developed a Motion-mode (M-mode) MSK-US paradigm employing sensors placed over muscles of interest to sense MSK tissue movement. Our miniaturized, wearable MSK-US enables rapid imaging via hands-free operation and is un-inhibiting to patient movement.

Methods: Participants performed a jumping task on a force plate with an MSK-US sensor attached to their right vastus lateralis (VL). Mean pixel value (MPV) and normalized pixel differences (NPD) were acquired from the images during the jumping task. Signals were filtered and normalized to root-mean square baseline and percent change was calculated for peaks of jump take-off and landing. The correlation coefficient was calculated to determine a relationship between metrics.

Results & Discussion: Force data showed that the mean ± SD of percent change during take-off and landing was 0.28%±0.09 and 0.66%±0.17 relative to baseline for each peak respectively. MPV values changed 0.42%±0.29 and 0.81%±0.17, and NPD changed 0.41%±0.32 and 0.84%±0.12 for corresponding peaks. Overall results indicated significant correlation between force data and MSK-US ($p < 0.05$). Our system can maintain acoustic coupling during complex movements providing real-time feedback and expanding the potential for wearable MSK-US sensors.

2.3. Vascular and Structural Assessment of Open Wounds Using Ultrasound Imaging. David Lemonnier[a], Brandon J. Sumpio[b], Ikram Mezghani[b,c], Maxwell Crouse[d], Georgios Theocharidis[b], Tengfei Ma[d], Aristidis Veves[b], Samuel K. Sia[e], Parag V. Chitnis[a], *[a]Bioengineering Department, George Mason University, Fairfax, VA 22030 USA, [b]Joslin-Beth Israel Deaconess Foot Center and The Rongxiang Xu, MD, Center for Regenerative Therapeutics, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215 USA, [c]Penn State University College of Medicine, Hershey, PA 17033 USA, [d]Thomas J. Watson Research Center, Yorktown Heights, NY 10598 USA, [e]Biomedical Engineering, Columbia University, New York, NY 10027 USA*

Background: Monitoring of wound healing progression is critical due to the risk of infection, non-healing wounds, or evolution towards a chronic state. In addition, there is a need to early identify healing deficiencies to adapt the treatments and reduce the current significant burden of wound management on healthcare. This study explores the application of ultrasound imaging to open wounds and the extraction of anatomical and vascular-related features in a longitudinal study.

Material and methods: 15 C57BL/6 mice received a 1cm-diameter full-thickness wound on their dorsum and were imaged using ultrasound from the surgical day (Day 0) to 25 days post-wounding. From the high frame rate, plane waves acquisitions with a 15 MHz transducer, image features based on pixels' texture and brightness levels were computed and compared to an automatic processing method. Singular Value Decomposition (SVD) filtering was also computed to provide vascular information.

Results: Our results indicate that the wounds closed during the third week post-wounding. The histogram peak value from the wound ROI remained increased from day 8, while echogenicity of the underlying tissue was temporarily higher from day 2 to day 10. Categorization of the wound open/closed condition with automatic positioning of the wound ROI was close from the manual selection. Vascularity Index

(VI) calculations showed a significantly increased vascular signal in the wound bed from day 6 to day 10 post-wounding compared to Day 0 ($p<0.05$). VI values were back to the basal level after 3 weeks. In comparison, no significant difference was highlighted for the vascular signal in the peri-wound area.

Conclusions: These results show that vascular ultrasound imaging can be applied to track anatomical and vascular changes of open wounds during the healing process. This approach may also be extended to other types of wounds for detecting early signs likely to cause complications.

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2.4. Quantitative Ultrasound Imaging of the Placenta in a Rat Model of Preeclampsia. Andrew Markel[1], Cameron Hoerig[2], Kenneth Swan[1], Allan Alancar[1], Carolyn Bayer[1], and Jonathan Mamou[2],*[1]Department of Biomedical Engineering, Tulane University, New Orleans, LA, [2]Department of Radiology, Weill Cornell Medicine, New York, NY, amarkel@tulane.edu*

Preeclampsia is a life-threatening pregnancy disorder that affects up to 10% of women in the United States. In preeclampsia, the spiral arteries in the placenta fail to remodel properly, consequently altering placental development, restricting fetal growth, and disrupting normal function of maternal organs. Preeclampsia is currently diagnosed by identifying high blood pressure and high concentrations of protein in the urine, but these symptoms indicate that the mother is already experiencing cardiovascular and renal malfunction. Early diagnosis of preeclampsia would allow interventions to avoid potentially life-threatening conditions for the mother and fetus.

Quantitative ultrasound (QUS) has the potential to diagnose preeclampsia non-invasively by assessing microstructural changes in the placenta. QUS parameters quantify tissue microstructure by modeling the backscattered coefficient and the envelope statistics from the radiofrequency signals.

QUS methods were investigated to diagnose preeclampsia in an established rat model of the condition. Radiofrequency ultrasound data were acquired from pregnant Sprague-Dawley rats on gestational days 14 and 18 using a Vevo 2100 imaging system equipped with an LZ550 transducer with 40MHz center frequency (FUJIFILM VisualSonics, Inc., Toronto, ON). On day 14, rats underwent reduced uterine perfusion pressure surgery to induce preeclampsia or sham surgery to serve as control.

Effective scatterer diameter (ESD) decreased by 3.22µm by day 18 ($p<0.05$). Homodyned-K k parameter increased by 0.08 ($p<0.05$). Increase in k corresponds with an increase in coherence of the echo signal, suggesting more structured organization of the scatterers. Nakagami m and Homodyned-K α increased by 0.15 ($p<0.05$) and 0.27 ($p<0.05$), respectively. An increase in these parameters suggests an increase in the scatterer number density.
We are developing QUS methods to detect longitudinal changes in placental microstructure during the development of preeclampsia. To our knowledge this is the first instance of QUS imaging of the placenta.

2.5. AIUM/QIBA Pulse-Echo Quantitative Ultrasound (PEQUS) Biomarker Committee update. I. M. Rosado-Mendez[1], M. Wang[2], A. Samir[3], and the members of the PEQUS biomarker committee (https://tinyurl.com/bdrwm7z9), *[1]Departments of Medical Physics and Radiology, University of Wisconsin, Madison, WI, [2]General Electric Healthcare, Wauwatosa, WI, [3]Center for Ultrasound Research & Translation, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, rosadomendez@wisc.edu*

Introduction: The AIUM/QIBA PEQUS committee's goal is to reach consensus on the technical performance (bias and variability) of the attenuation coefficient, the backscatter coefficient, and the speed of sound used as biomarkers of hepatic steatosis in the context of non-alcoholic fatty liver disease. This presentation will describe the progress and challenges of the committee's work.

Methods: Members performed extensive literature reviews on the performance of the biomarkers for the assessment of liver steatosis. In parallel, the committee defined the specifications for phantoms mimicking the acoustic properties of normal and steatotic liver to test biomarker bias and variability in a round-robin study.

Results: The literature reviews have been reported in four publications (3 published, 1 under review). Two sets of phantoms have been produced and shipped to the first sites of the round-robin study. To assess biomarker bias, the reference values of the phantom materials are being characterized using water-tank-based techniques. Challenges include addressing the physical and technical aspects of biomarker quantification and organizing data collection for the phantom study.

Conclusions and future work: A new working group will produce the first version of the biomarker profile describing claims of expected levels of bias and variability. At the end of the phantom study, the claims will be refined based on the study findings.

Acknowledgements: We thank industry partners for technical and financial support, and Mirion Technologies for the donation of the tissue mimicking phantoms.

2.6. Predicting Head and Neck Cancer Treatment Outcomes Using Machine Learning Classifiers Trained with Features from Pre-treatment Lymph Node Ultrasound and CT Scans. Safakish, A.[1,2], Sannachi, L.[1], DiCenzo D.[1], Kolios, C.[1,2], Pejović-Milić, A.[2] Czarnota, G.J[1-3], *[1]Department of Radiation Oncology, and Physical Sciences, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [2] Department of Physics, Toronto Metropolitan University, Toronto, ON, Canada, [3]Departments of Medical Biophysics, University of Toronto, Toronto, ON, Canada, Gregory.Czarnota@sunnybrook.ca*

Objectives: Cancer treatment and associated side-effects can be challenging for patients. Clinicians justify prescribing treatment by considering potential benefits. An accurate, reliable, and convenient method of predicting cancer treatment outcomes would provide an excellent tool for physicians in pursuit of optimal personalized patient care. Radiomics is the extraction of texture-related features from biomedical images to gain further insight regarding phenotypic information otherwise invisible to the naked eye. Radiomics features can be used to train machine learning (ML) algorithms to predict a plethora of clinical endpoints.

Methods: Ultrasound (US) and computed tomography (CT) scans were acquired for head & neck (H&N) cancer patients (n = 72) prior to starting treatment. Patients were retrospectively labelled as complete or partial responders as determined by physician three months after treatment completion. Lymph node (LN) regions of interest (ROIs) were segmented. 476 QUS and 136 CT features were determined. Two classifiers (k-NN & SVM) were used to create predictive models with 1-7 features.

Outcomes: A SVM outperformed a k-NN classifier for both QUS and CT features. Models trained on QUS features outperformed models trained on CT features. The best (SVM classifier trained with QUS features) and worst model (k-NN classifier trained on CT features) found sensitivity (81% vs. 48%), specificity (76% vs. 61%), accuracy (79% vs. 65%) and precision (86% vs 40%), respectively. Findings suggest that QUS features are more informative than CT features for comparable patient sample sizes and that acoustic and radiologic phenotypic difference between H&N cancer patient LNs may reveal insight about future response to treatment.

3. Imaging Session

3.1. Emulating Clinical Muscle B-modes Using a Two Stage Machine Learning Model. Reed Chen, Courtney Trutna Paley, Wren Wightman, Lisa Hobson-Webb, Felix Jin, Ouwen Huang, Mark Palmeri, Kathryn Nightingale *Duke University, reed.chen@duke.edu*

Research ultrasound scanners such as the Verasonics Vantage often lack the advanced image processing algorithms used by clinical systems, and traditional image-processing algorithms are relatively slow. Thus, attempting to achieve clinical-grade images on research scanners is not only difficult, but often results in a severe loss in framerate. Plane-wave compounding is another method commonly used to improve the quality of ultrasound images. However, the more plane waves that are compounded, the slower the framerate.

Here, a two-stage machine learning algorithm was developed to improve real-time image processing of muscle B-mode images – a complex task due to the echogenic and transversely isotropic fibers in muscle. The input to the model is a single plane wave image, and the model's output is an image that emulates the image

quality from clinical ultrasound scanners. The first stage consists of a U-Net trained using paired images. Ground truth images were obtained by processing the plane-wave compounded (PWC) image using a traditional image processing pipeline selected by a clinician. The second stage consists of a CycleGAN and was trained using the ground truth images of the first stage and clinical muscle B-mode image datasets from on-line repositories.

This model was implemented on the Verasonics Vantage ultrasound scanner to provide high-speed image formation at clinical quality from a single planewave transmit. Our results showed that the model was able to produce images comparable to PWC images from a single plane wave. Additionally, model inference was faster than using a traditional algorithm. The output images of the model qualitatively resembled clinical ultrasound images, demonstrating the utility of machine learning for real-time muscle B-mode enhancement.

3.2. Ultrafast ultrasound beamformer for plane wave imaging with field programmable gate array. Zhengchang Kou, Michael L. Oelze, *ECE, University of Illinois Urbana-Champaign (UIUC), Beckman Institute for Advanced Science and Technology, UUC zkou2@illinois.edu; oelze@illinois.edu*

In this work, we propose a novel method of implementing an ultrafast ultrasound beamformer for plane wave imaging (PWI) on a field programmable gate array (FPGA). First, a modified delay calculation method was proposed to: 1) separate the transmit and receive delays, 2) reduce the size of delay profile, and 3) enable parallel beamforming by delay reuse and data vectorization. Second, a parallelized implementation of beamformer on single FPGA was proposed by: 1) loading a pre-calculated delay profile from external memory instead of calculating delays during run-time, 2) vectorizing the fetching of channel data, 3) compensating transmit and receive delays separately, and 4) using fixed summing networks to reduce consumption of logic resources. The proposed method was also highly scalable, which was demonstrated by implementing the beamformer with different beamforming rates in terms of input raw RF data samples ranging from 1.2 G to 4.8 G samples per second to three different sizes of FPGAs ranging from entry-level FPGA to high-end FPGA. The power consumption was less than 6 watts for a 2.4 G samples per second beamforming rate, which demonstrates the possibility of implementing ultrafast ultrasound imaging on a handheld ultrasound probe. The FPGA beamformer's results were compared with Verasonics CPU beamformer's result to verify that the image quality was not compromised for speed.

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3.3. Distributed Aberration Correction for Transcranial Doppler: A Simulation Study using a High Sound Speed and Density Aberrator. Saachi Munot, Thurston Brevett, Jeremy Dahl, *Stanford University, Department of Radiology, Stanford, California USA, saachim@stanford.edu*

Introduction and Background: The widespread application of transcranial Doppler and related methods, including functional ultrasound imaging, are limited by distortion effects of the skull that are not entirely accounted for by general beamforming methods and near field aberration correction methods. Alternatively, frequency domain distributed aberration correction methods, such as the wavefield correlation method (Ali et al [1]), that account for the diffractive and refractive effects of wave propagation have shown promise in imaging through aberrators. This study aims to investigate the effect of wavefield correlation in both the time and frequency domain in the context of Doppler imaging specifically through a high contrast aberrator.

Methods: We implemented a frequency domain (modified version of Ali et al [1]) and time domain wavefield correlation beamformer for plane wave transmisions (11 angles, -10 to 10 egrees) for distributed aberration correction. In this method we compute a cross correlation of the transmitted and received pressure wavefields over all time or over all frequencies to create an image. We placed a point scatterer underneath the strong aberrating region at a depth of 2.5 cm to evaluate the point spread function (PSF). To apply the method to Doppler ultrasound, we simulated blood flow in a vessel underneath the planar skull aberrator (c = 2500-3000 m/s, rho = 1500-2000 kg/m^3, thickness = 0.75-2 cm). We then performed Doppler processing (PRF 500, ensemble length >= 50) with the wavefield correlation beamformed images.

Results and Conclusions: For conventional delay-and-sum beamforming, we obtained a full width half max (FWHM) of ~1 mm for the mainlobe. We achieved a FWHM of ~0.3 mm for the mainlobe for plane wave transmits computed using both the time domain and frequency domain wavefield correlator. As a comparison, the FWHM for the same simulation medium computed with eikonal delays and full synthetic aperture transmit was ~0.25 mm . Moreover, based on preliminary results, there is an improvement in the accuracy and spatial sensitivity of the power Doppler signal. This suggests using wavefield correlation beamforming method improves the sensitivity of transcranial doppler.

References: [1] Ali, R.; Hyun, D.; Brickson, L.; Dahl, J. "Distributed Aberration Correction Techniques Based on Tomographic Sound Speed Estimates". IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control (2022).

3.4. Plane Wave Imaging in Arbitrary Media via Efficient Phase Compensation. Scott Schoen Jr,[1] Marko Jakovljevic[1], and Anthony E. Samir[1], *[1]Center for Ultrasound Research and Translation, Harvard Medical School and Massachusetts General Hospital, Boston, MA USA, sschoenjr@mgh.harvard.edu*

The development of plane wave (PW) compounding beamforming for ultrafast ultrasound (US) imaging has enabled the noninvasive visualization of transient (millisecond scale) phenomena. Such high temporal resolution is vital for applications such as shear wave elastography, ultrafast Doppler, and perfusion imaging. However, PW imaging usually relies on coherence of waves assuming homogeneous propagation; in the presence of heterogeneities (e.g., fat and muscle layers overlying soft tissue), this coherence is degraded, and the result is reduced image quality. Addressing unknown aberration typically requires computationally expensive manipulation of time series channel data, and compensating for a known environment (e.g., time reversal) entails similarly costly simulation.

Here, we show that the recently proposed heterogeneous angular spectrum method (HASM), which operates directly in plane wave space, may be used for direct calculation of broadband corrective transmit delays. Through k-Wave simulations in media with arbitrary, spatially-varying speeds of sound, HASM demonstrated a 68.7±20.5% reduction in the phase error at the target depth compared to the uncorrected case, over a range of transmit angles (±15°), mean speed of sound variations (2% to 15%) and transmit frequencies (0.5 to 2 MHz). Computing the corrections required 53.0±0.5 ms per angle, compared with 8.40±0.03 s for the equivalent time domain simulation to compute the phase and amplitude variations (150-fold faster). Importantly, HASM scales trivially to 3D for application to emerging 2D arrays and volumetric imaging, wherein the computational complexity of simulation becomes especially prohibitive. HASM thus represents an important tool towards aberration correction and improved visualization of transitory phenomena in heterogeneous media.

Tuesday Morning June 6th

4. Quantitative Ultrasound, Breast Applications Session

4.1. Radiomics of Quantitative Ultrasound (QUS) Spectral Parametric Imaging for the Non-Invasive Characterization of Breast Lesions. Laurentius O. Osapoetra[1], Lakshamanan Sannachi[1], Schontal Halstead[1], David Alberico[1], Joyce Wai Sze Yip[1], Michael Oelze[2], and Gregory J. Czarnota[1,3], *[1]Department of Radiation Oncology, and Physical Sciences, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [2]Department of Electrical and Computer Engineering, University of Illinois Urbana-Champaign, IL, U.S.A., [3]Departments of Medical Biophysics and Radiation Oncology, University of Toronto, Toronto, ON, Canada. Gregory.Czarnota@sunnybrook.ca*

Objectives: Accurate and timely diagnosis of breast cancers is very crucial because of its high incidence and high morbidity. Development of diagnostic imaging techniques for rapid and accurate characterization of breast lesions is required. We demonstrate the clinical utility of a radiomics strategy on QUS spectral parametric images for breast tumour characterization.

Methods: The cohort consists of 317 patients with breast lesions (107 benign and 210 malignant). Parametric images of mid-band-fit (MBF), spectral-slope (SS), spectral-intercept (SI), average scatterer diameter (ASD), and average acoustic concentration (AAC) from raw US radiofrequency (RF) data were generated. Radiomics features that include first-order statistical, morphological, and texture features from tumour core and its 5-mm tumour margin were determined utilizing a gray level co-occurrence matrix (GLCM), gray level run-length matrix (GRLM), gray level size-zone matrix (GLSZM), gray level dependence matrix (GLDM), and neighbouring gray tone difference matrix (NGTDM) to quantify image textures. A multi-variate classification model with target labels provided from histopathology was developed using randomly divided samples into a stratified 80%-20% development-test set for model building and evaluation, repeated a hundred times. A five-fold cross-validation (CV) on the development set to fine-tune and select an optimum model was used. The performance of several classifiers including linear discriminant analysis (LDA), nearest neighbours, support-vector-machines (SVM), boosting, and a shallow artificial neural network (ANN) was compared.

Results: LDA attained the best classification performance of 88% sensitivity, 82% specificity, 85% balanced accuracy, and 0.92 AUC on an independent test set. On average, LDA and SVM-Linear obtained test classification performance of 75%±8% recall, 79%±9% specificity, 77%±5% balanced accuracy, and 0.85±0.04 AUC.

Conclusions: Radiomics-based framework of QUS spectral parametric images enables accurate classification of breast lesions on a larger cohort of patients and provides a foundation for the use of QUS spectroscopy radiomics in the characterization and differentiation of breast lesions.

4.2. A priori prediction of tumor response to neoadjuvant chemotherapy in breast cancer patients using quantitative ultrasound, texture and molecular subtype. Lakshmanan Sannachi[1], Laurentius O. Osapoetra[1], Schontal Halstead[1], Sonal Gandhi[2], Frances Wright[3], Michael Oelze[4] and Gregory J. Czarnota[1,5], *[1]Department of Radiation Oncology, and Physical Sciences, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [2]Division of Medical Oncology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [3]Division of General Surgery, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [4]Department of Electrical and Computer Engineering, University of Illinois Urbana-Champaign, IL, U.S.A., [5]Departments of Medical Biophysics and Radiation Oncology, University of Toronto, Toronto, ON, Canada. Gregory.Czarnota@sunnybrook.ca*.

Objective: In this study, we have demonstrated improvement in breast cancer response prediction to neoadjuvant (NAC) before treatment by combining quantitative ultrasound (QUS), texture, texture-derivative, tumor-margin analyses, and molecular subtype, with machine learning approach.

Patient and Methods: Ultrasound data were collected from 208 LABC patients before chemotherapy treatment. Five QUS parametric images were generated from tumour core and a 5-mm tumour margin regions. Gray Level Co-Occurrence Matrix (GLCM) based texture maps were created from each QUS parametric images to quantify their heterogeneities. A total of 201 features including mean QUS, image quality, texture and texture derivative parameters were determined from those QUS and texture images. Each breast cancer's molecular subtype was defined based on hormone receptor status. Patients were classified into two treatment response group based on a modified response grading system. Two multi-features response prediction algorithms using a k-nearest neighbour and support vector machine were developed. Leave-one out and hold-out cross-validations were used to evaluate response-prediction model performance.

Results and Discussion: In a leave-one out approach, the QUS-texture analysis based SVM model attained good classification performance with 80% accuracy and AUC of 0.83. Including molecular subtype in the classification model improved the performance to 83% accuracy and 0.87% of AUC. Hold-out cross validations were performed with 10% and 20% data used for testing. Classification performance with 90% training was approximately similar to those with leave-one out approach. However, due to limited sample size, a model developed with 80% training exhibited poorer performance. The most relevant features selected for predicting the treatment response groups were from image quality, texture derivative, and molecular subtype.

Conclusion: Treatment response can be predicted accurately at an individual subject level by combining quantitative ultrasound, tumour-margin texture derivative with molecular subtype and guide the treatment planning of refractory patients.

4.3. Quantitative Noninvasive Texture Analysis of Breast Masses in Ultrasound Images: Proposal of a New Gold Standard. Sleiman R. Ghorayeb,[1,2,3] Rena Fukuda,[2] and Mirla Sales[2], *[1]School of Medicine at Hofstra/Northwell and [2]School of Engineering and Applied Sciences, Ultrasound Research Laboratory, Hofstra University, [3]Department of ObGyn/MFM at Northwell Health. Sleiman.R.Ghorayeb@hofstra.edu*

Breast cancer is diagnosed after imaging workup and image-guided biopsy of breast lesions, often under ultrasound (US) guidance. However, the nature of breast lesions is often difficult to determine based on imaging characteristics alone. The goal of this research study is to examine the utility of novel quantitative sonographic indices, the percent echogenicity (%Echo) and heterogeneity index (HI), which may aid in more accurately and noninvasively determine benignity or malignancy of breast lesions based on ultrasound imaging alone. Also, we aim to determine an optimal %Echo threshold to predict malignancy of breast masses. This protocol has the potential to be incorporated into standard clinical practice.

Assessment was done retrospectively on a total of 217 cases of fibroadenoma (FA) and malignant invasive ductal carcinoma (mIDC) for which targeted ultrasound evaluation was performed. There was an expected observed significant difference in average %Echo when comparing FA and mIDC masses (20.83 vs 11.70, $p<0.00005$). When comparing the ratio of average %Echo of the surrounding fat with those of FA and mIDC, there was also an observed difference (3.07 vs. 8.07) and a percent change between adjacent fat and FA and mIDC (42.1 vs 74.3, $p<0.000001$). Interestingly, there was no significant difference when assessing the HI of these masses (average of 1.85 for both). However, there was a cross-correlated significant difference in average HI values obtained in fat surrounding FAs and mIDCs (1.58 vs 1.37, $p<0.00005$). ROC curve revealed an area under the curve of 0.949, with a sensitivity of 84% and a specificity of 100%. An optimal %Echo threshold value of ≥11.88 was determined as the predictor of malignant breast masses.

If such a technique is implemented into clinical practice, it may have a significant impact in predicting benign versus malignant lesions with the potential of providing accurate and reliable prognostic information.

4.4. Comparison of Quantitative Ultrasound and Computed Tomography Radiomics with Texture-Derivative Features for Breast Cancer Response Prediction. Deok Hyun Jang[1,2], Lakshmanan Sannachi[1], Laurentius O. Osapoetra[1] and Gregory J. Czarnota[1-3], *[1]Department of Radiation Oncology, and Physical Sciences, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [2]Department of Physics, Toronto Metropolitan University, Toronto, ON, Canada, [3]Departments of Medical Biophysics, University of Toronto, Toronto, ON, Canada. Gregory.Czarnota@sunnybrook.ca.*

Objectives: Breast cancer response to neoadjuvant chemotherapy (NAC) is associated with better survival outcome. In this study, we compare the response prediction performance of prediction models that utilize radiomic features from quantitative ultrasound (QUS), magnetic resonance imaging (MRI) and computed tomography (CT).

Methods: Pre-treatment QUS, MRI and CT images were acquired from 177 breast cancer patients, respectively. Tumour core and 5mm tumour periphery were delineated for both sets of images. In addition, five QUS parametric images of mid-band fit (MBF), spectral slope (SS), spectral intercept (SI), average scatterer diameter (ASD), and average acoustic concentration (AAC) were generated from the original QUS image. Texture features were extracted from the original and the parametric images, and the texture feature maps were generated. Texture-derivative features were determined for quantification. These texture and texture-derivative features along with hormone receptor status were used to classify patients as responders and non-responders, where responders are defined as patients who achieved tumour size reduction greater than 30% after NAC. The dataset was split into an 80% training set and a 20% hold-out test set, and the predictive performance was evaluated on the test set.

Outcomes: Using a shallow neural network classifier, CT and MRI analysie yielded accuracies of 77% and 75%, and AUCs of 88% and 76% in the test set Using a support vector machine (SVM) classifier, QUS analysis exhibited a best accuracy of 83% and AUC of 87% for the response prediction in a test set. For CT, MRI and QUS models, the majority of the features selected for the prediction were from the texture-derivative feature sets, in addition to the hormone receptor status. In conclusion, this study demonstrates the usefulness of texture-derivative features from QUS, CT and MRI with concordance regarding performance for NAC response prediction in breast cancer patients.

4.5. Quantitative Ultrasound Texture Analysis of Breast Tumors: Comparison of Portable and Cart-Based Ultrasound Scanners. David Alberico[1], Daniel DiCenzo[1], Schontal Halstead[1], Joyce Yip[1], Lakshmanan Sannachi[1], Sonal Gandhi[2], Frances Wright[3], Michael Oelze[4], and Gregory Czarnota[1,5], *[1]Department of Radiation Oncology, and Physical Sciences, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [2]Division of Medical Oncology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [3]Division of General Surgery, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [4]Department of Electrical and Computer Engineering, University of Illinois Urbana-Champaign, IL, U.S.A., [5]Departments of Medical Biophysics and Radiation Oncology, University of Toronto, Toronto, ON, Canada. Gregory.Czarnota@sunnybrook.ca*

Objectives: Quantitative ultrasound (QUS) and texture analysis techniques have been shown to be effective methods for predicting the treatment response of locally advanced breast cancer (LABC) to neoadjuvant chemotherapy (NAC). In order to better apply these methods in a clinical context, it is desirable that there be good agreement between estimates of QUS parameters and texture features acquired using different devices. Handheld ultrasound imaging systems are of particular interest for clinicians as they are compact, relatively inexpensive, and highly portable. In this study, we investigated the agreement between the QUS and texture parameters estimated from breast tumor images acquired using the two system types.

Methods: A total of 43 patients with malignant breast lesions were included. Breast tumours were imaged using an Ultrasonix RP (ULX), (cart-based), and the Clarius (portable) ultrasound systems prior to any treatment or surgery. QUS parametric images were generated from the tumor core and a 5 mm tumor-margin regions from ultrasound radio frequency (RF) data using QUS techniques. Four texture images were created from QUS maps using the gray-level co-occurrence matrix (GLCM) texture analysis method. Additional texture-derivative features were then extracted from these texture maps by applying the GLCM technique a second time. The root mean square differences (RMSD) between parameter estimates from the two systems were calculated to quantify the level of agreement between the systems.

Results & Discussion: The RMSD calculated for all QUS, texture, and texture derivative parameters between the two systems indicated only small variations in parameter estimates. Data including backscatter power spectra and backscatter-related QUS parameters and response predictions made were effectively equivalent.

Conclusion: The results demonstrate good agreement between the imaging systems and support a case for further investigation of using portable QUS-enabled ultrasound systems for breast cancer treatment response prediction.

4.6. Transfer Learning of Pre-treatment Quantitative Ultrasound Images for the Prediction of Locally Advanced Breast Cancer Response to Neoadjuvant Chemotherapy. Omar Falou[1,2], Lakshmanan Sannachi[3,4,5,6], Gregory J. Czarnota[3,4,5,6], Michael C. Kolios[1,2], *[1]Department of Physics, Toronto Metropolitan University, Toronto, Ontario, Canada, [2]Institute for Biomedical Engineering, Science and Technology (iBEST), Keenan Research Centre for Biomedical Science, St. Michael's Hospital, Toronto, Ontario, Canada, [3]Department of Radiation Oncology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [4]Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada, [5]Physical Sciences, Sunnybrook Research Institute, Toronto, ON, Canada, [6]Department of Medical Biophysics, University of Toronto, Toronto, ON, Canada, ofalou@torontomu.ca*

Breast cancer is the most common malignancy for females in North America. Approximately 5-15% of the estimated 282,000 new cases diagnosed yearly in the US will present with locally advanced breast cancer (LABC). Women with LABC have an inferior outcome in both local and systemic recurrence. Standard treatment for these patients is usually neoadjuvant systemic therapy followed by surgery and radiotherapy. The necessity for a non-invasive and inexpensive imaging modality to diagnose and predict treatment response has led to renewed interest in the potential of quantitative ultrasound. This study investigated a novel transfer learning-based approach to predict LABC response to neoadjuvant chemotherapy using QUS imaging at pre-treatment. QUS parametric images of breast tumors with margins were generated using data from 174 patients. For each patient, the ground truth response to therapy was based on the standard clinical and pathological criteria. The ResNet50 deep learning architecture was used to extract features from the parametric maps. This was followed by feature selection and data balancing processes using SelectKBest and Synthetic Minority Over-sampling techniques, respectively. The Support Machine (SVM) algorithm was employed to categorize patients into two distinct groups: responders and nonresponders. Evaluation results on an independent test set demonstrate that transfer learning-based approach using spectral slope parametric maps had the best performance in response prediction with recall, precision, and balanced accuracy of 100%, 93%, and 86%, respectively. The transfer learning-based approach has many advantages over conventional deep learning methods since it reduces the need for large image datasets for training and shortens the training period. The results of this study demonstrate the potential of transfer learning in predicting LABC response to neoadjuvant chemotherapy prior to the start of treatment using quantitative ultrasound imaging.

5. Flow Measurement Session

5.1. From literature to implementation: Challenges in the development of a calibrated microflow phantom.

Lizbeth Ayala-Dominguez,[1] Kricia Ruano Espinoza,[2] and Ivan Rosado-Mendez[1], *[1]Department of Medical Physics, University of Wisconsin - Madison, Madison, WI, USA, [2]Department of Radiology, University of Wisconsin - Madison, Madison, WI, USA.* lizbeth.ayaladominguez@wisc.edu

Reference standards are fundamental for validating quantitative imaging biomarkers and microvasculature ultrasound imaging methods. Here we describe the development of a calibrated microflow phantom and the challenges on achieving channels and flow velocities suitable for studying microvessels.

Wall-less channels with nominal diameters dn = 203, 150, and 100 µm, were cast in an agar-based tissue-mimicking material (TMM) [1]. A blood-mimicking fluid (BMF) [2] was perfused through the channels using a microfluidic pressure controller (15-300 mbar). Flow rate was measured using timed weight collection (3 repetitions); the relationship between pressure and flow rate was evaluated. Flow velocity was estimated from the flow rate and dn. Slow-flow Power Doppler response was evaluated with a Siemens Acuson Sequoia scanner (Siemens Healthcare, Mountain View, CA, USA) using a 18L6 transducer by measuring channel diameter (dm) from mask images created with color filter in HSV space.

We have completed characterization of the channel with dn = 203 µm. A linear relationship (R2 = 0.99) was found between pressure and flow rate. Flow rate and flow velocity ranged from 3-400 µL/min and 3-200 mm/s, respectively. The coefficient of variation among repetitions was 2.9 ± 2.2%. An average dm = 1.48 ± 0.3 mm was found in the slow-flow Power Doppler images; dm increased with pressure and it could be affected by blooming artifacts. The other channels could not be evaluated due to unexpected clogging. Current efforts are being carried out to overcome the challenges found for vessel diameter reduction, and to acoustically characterize the TMM and BMF. In the long term, the developed microflow phantom could be used in the validation of methods for microflow assessment with ultrasound.

Funding for this project was provided by the UW School of Medicine and Public Health from the Wisconsin Partnership and the Centennial Scholars programs.

[1] Grand-Perret, V. et al. A Novel Microflow Phantom Dedicated to Ultrasound Microvascular Measurements. Ultrason Imaging 40, 325–338 (2018).

[2] Ramnarine, K. V., Nassiri, D. K., Hoskins, P. R. & Lubbers, J. Validation of a new blood-mimicking fluid for use in Doppler flow test objects. Ultrasound Med Biol 24, 451–459 (1998).

5.2. Contrast-free Peripheral Perfusion Imaging in the Diabetic Ischemic Mouse Hindlimb. Somaye Babaei, Bingze Dai, Wawrzyniec L. Dobrucki, Michael F. Insana. *mfi@illinois.edu. Department of Bioengineering, University of Illinois at Urbana-Champaign, Urbana IL 61801*

Peripheral artery disease (PAD) is a prevalent pathological condition characterized by atherosclerotic plaques that impede blood flow in the arteries and arterioles of the lower limbs. Currently, the clinical assessment of PAD entails measuring the ankle-brachial index (ABI). Patients failing the ABI test are followed by magnetic resonance imaging (MRI) or computed tomographic (CT) angiography to search for arterial occlusions. However, interpreting ABI values can be challenging in older patients, and endothelial dysfunction, a robust predictor of plaque formation, is difficult to detect using current diagnostic methods.

Our study aims to evaluate the sensitivity and specificity of power-Doppler ultrasound (PD-US) in detecting muscle perfusion changes in a unilateral ischemic hindlimb model developed for use in healthy and diabetic mice. We monitored perfusion patterns in ischemic muscle relative to the contralateral control hindlimb in eight groups over four weeks, including male and female mice who were healthy or diabetic and either sedentary or exercise-conditioned. We collected the data using a 24 MHz ultrasound transducer, followed by Laser Speckle Contrast Imaging on both hindlimbs.

We found that spatial registration applied before PCA clutter filtering was highly effective at isolating the perfusing blood signal. While we found there to be little difference between males and females, the angiogenic recovery time in diabetic mice increased to 9-10 days compared with the 5-6 days found for healthy animals. Exercise conditioning reduced recovery time an average of one day relative to sedentary animals. Our findings demonstrate the potential of PD-US methods in monitoring gradual changes in peripheral muscle perfusion over time. Consequently, with modest software changes, PD-US can be applied to PAD patients to monitor progression and responses to treatment regularly.

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5.3. Improved resolution and contrast for ultrafast power Doppler microvessel imaging with null subtraction imaging. Michael L. Oelze, Zhengchang Kou. *ECE, University of Illinois Urbana-Champaign (UIUC), Beckman Institute for Advanced Science and Technology, UUC. oelze@illinois.edu*

In this work, we demonstrate a novel non-linear beamforming technique, called null-subtraction imaging (NSI), to improve spatial resolution and image contrast of ultrafast, power Doppler microvessel imaging without significantly increasing computational cost compared to traditional delay and sum (DAS). NSI is a non-linear beamforming technique that operates on receive data by subtracting envelopes of beamforming results from three apodization windows. An array transducer and Verasonics Vantage 256 system were used to capture 1,600 frames of raw ultrasonic radio frequency (RF) channel data by scanning a rat brain using nine plane waves spanning angles between -4° and 4° at a pulse repetition frequency of 1,000 Hz. A Singular Value Decomposition filter was applied on the raw RF channel data to filter out the tissue signal. Coherent compounding was performed individually on the beamformed result for each apodization window. Next, the subtraction of the envelopes for each apodization was conducted to form the NSI image. A total of 1,600 frames of NSI images were accumulated to form the final image. The NSI based ultrafast power Doppler microvessel imaging provided a ten-fold improvement in spatial resolution and a three-fold improvement in image contrast compared with the traditional DAS-based ultrafast power Doppler microvessel imaging.

This work was supported by grants from the NIH (R21EB24133, R01CA273700 and R01CA251939).

5.4. Value of Long-Ensemble Power Doppler to Detect Slow Flow in Metastatic Renal Carcinoma (mRCC). Sergio J Sanabria[a], Neha Antil[a], Christian Horner[a], You Leo Li[a], Aya Kamaya[a], Susanna Miao[a], FeiFei Qin[a], Max Zalcman[a], Alice Fan[a], Jeremy Dahl[a], *[a]Stanford University, Stanford, California USA, sanse@stanford.edu*

Background: Limitations exist in the ability of clinical Power Doppler (PD) to detect slow flow in small-diameter vasculature in metastatic renal carcinoma (mRCC). Ultrafast-Doppler imaging sequences (UFPD) can be used to increase ensemble length. Recently, a LEAD PD sequence has been proposed, which exploits the coherence of the RF signal for long-ensemble PD reconstruction. Here we comparatively assess the diagnostic value of these sequences for mRCC.

Methods: A population of 15 patients scheduled for a combination of antingionenesis and immunotherapy mRCC treatment was recruited over 24 months. Ultrasound basal exams and after 3 and 6 weeks of treatment were performed. Real-time clinical PD was acquired with a Siemens S2000 system. A Verasonics research scanner with harmonic B-mode navigation was used to reconstruct UPFD and LEAD offline (ensemble length 3s, 500 Hz). For lesion depths < 40 mm a 7.5 MHz linear transducer and for larger depths a 3.0 MHz curvilinear probe were used. A trained radiologist independently analyzed each image for internal lesion flow (1a), peripheral flow (1b) or no flow (0).

Results: The lesion depth ranged from 1-11cm:(mean=4.9) and the lesion diameter 0.43-11.22cm:mean=3.25. The distribution of flow detection was 1a(50%), 1b(25%) and 0(25%). Out of 56 lesion exams, 9/38 showed diagnostic superiority with long-ensemble sequences and 38/56 equal diagnostic performance. LEAD showed diagnostic superiority in 13/59 cases and PD in 3/59 cases, while in 43/59 cases they were equivalent. Overall, long-ensemble provided better mRCC flow resolution and detected a larger amount of vessels, while flow detection was limited by offline reconstruction and cluttering of adjacent tissue sources. LEAD was less sensitive to artifacts (movement, reverberation, poor-coupling) and showed higher vessel resolution, while UPFD showed better sensitivity.

Conclusions: Long-ensemble sequences add clinical value to renal HCC diagnostics, with LEAD being more robust and showing smaller flow detail than conventional UFPD.

Tuesday Afternoon June 6th

6. Photoacoustics Session

6.1. Modular photoacoustic helmet for vulnerable neonatal monitoring in NICU. Ananya Tandri, Jeeun Kang, Emad M. Boctor. *Johns Hopkins University, Baltimore, MD 21218. kangj@jhu.edu; eboctor@jhu.edu*

Neonatal encephalopathy can arise from fetal hypoxia-ischemia during labor, chronic uteroplacental inflammation, and large cerebral artery embolization primarily arising from dislodgement of a placental thrombus. Because of overlapping clinical presentation, differential diagnosis is often delayed until seizures develop, and MRI can be safely performed, a time at which most neuroprotectants are ineffective. Whereas hypothermia is approved for use within 6 hours of birth for hypoxia-ischemia, no treatments have been approved for perinatal arterial ischemic stroke because of the difficulty of definitive diagnosis required for clinical trial stratification at birth. With an estimated incidence of 17-93 per 100,000 live births, the incidence of stroke in the perinatal period rivals the incidence of stroke in adults (17-23 per 100,000). Therefore, a device that could rapidly and reliably identify an area of focal cerebral ischemia soon after birth would have a major impact by enabling the testing of neuroprotectants at an early therapeutic time window that would maximize efficacy. In this abstract, we propose a photoacoustic helmet (PAH) device that can be safely deployed at the bedside in the neonatal intensive care unit to 1) continuously monitor and rapidly identify at-risk neonates with different head shapes, shortly after birth, rapidly allowing them to be triaged to therapy; 2) monitor the progress of therapy; and 3) provide prognostic information to the parents of newborns at risk for life-long brain injury. In this abstract, we present the initial simulation results that validate the feasibility of the modular PAH device.

6.2. Towards MRI-compatible photoacoustic imaging of prostate cancer: Instrumentation evaluation. Ryo Murakami[1], Yang Wang[1], Ryosuke Tsumura[2], Yichuan Tang[1], Yasuyuki Tsunoi[3], Christopher J. Nycz[1], Wojciech G. Lesniak[4], Martin G. Pomper[4], Gregory S. Fischer[1], and Haichong K. Zhang[1], *[1]Worcester Polytechnic Institute, the United States, [2]National Institute of Advanced Industrial Science and Technology, Japan, [3]National Defense*

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Prostate cancer (PCa) is a significant public health concern. The timely screening and monitoring of PCa are critical for the effective treatment and management of the disease. However, the currently available imaging techniques, such as Ultrasound (US) and Magnetic Resonance Imaging (MRI), have limited capabilities in functional imaging, which is important for screening and monitoring PCa.

To address this, we propose integrating photoacoustic (PA) imaging with US and MRI to provide complementary imaging of PCa. PA imaging is known for its expertise in functional imaging such as a selective visualization of molecularly targeted contrast agents, which can facilitate the classification of cancers according to aggressiveness.

In this report, we describe the development and evaluation of a PA/US probe which we specifically designed for usage inside the MRI bore, where its electromagnetic field exists. The probe was intentionally constructed without magnetic substitute components and with minimal use of metallic materials. As a phantom, three tubes were prepared with different mixing conditions of two contrast agents, 25µM ICG with water, and an MRI marker to simulate the scenarios where only the multi-wavelength PA imaging can differentiate between the solutions.

The results of our study show that PA imaging could differentiate each solution based on its spectrum. These findings confirm the feasibility of the proposed complementary tri-modal imaging for the screening and monitoring of PCa.

6.3. Miniaturized Intracardiac Photoacoustic Imaging Catheter: Below 4 mm Diameter. Shang Gao, Ryo Murakami, Haichong K. Zhang, *Worcester Polytechnic Institute, Worcester, MA, 01609, hzhang10@wpi.edu*

Radiofrequency (RF) ablation is a minimally invasive therapy used to treat heart arrhythmia, such as atrial fibrillation (A-fib). This technique creates lesions by applying an electric current to isolate the heart from abnormal electrical signals. Photoacoustic (PA) imaging is an emerging imaging modality based on laser-generated ultrasound (US), which provides real-time feedback of the ablation process based on the tissue spectrum changes during ablation. PA imaging has unique advantages over conventional CT or MRI for this purpose. However, miniaturized PA imaging devices reported previously have limited imaging areas due to light-acoustic alignment or lack of maneuverability through the vessel. Therefore, an integrated catheterized PA imaging device with tip-bending navigation capability is critical for implementing PA monitoring in cardiac ablation procedures. Here, we propose a miniaturized phased-array intracardiac PA imaging catheter that integrates all components under a 4 mm diameter with flexible tips that allow it to navigate through the vessels. Two side-diffusing fibers were attached to the intracardiac echocardiography (ICE) US catheter to design the proposed PA catheter. The catheter has two active degree-of-freedom (DoF) bending tips, enabling it to navigate through the vessel to approach the heart. The diffusing fibers were aligned parallel to the US sensing array, allowing illumination across the entire imaging region. All the components were mounted by a customized 3D printed holder and packaged in a soft silicon tube with an outer diameter of 4 mm. We conducted a phantom study with a nylon wire phantom designed with a pattern in 3D space to validate the imaging capability of the proposed imaging catheter. The image quality of 0.53±0.03 mm resolution and 25.45±2.28 dB signal-to-noise ratio was achieved on 0.2 mm diameter targets located 9.5 mm depth. The results successfully demonstrated the feasibility of the proposed intracardiac PA imaging catheter providing high quality imaging.

6.4. Development of mechanical property microscopy using photoacoustic excitation and optical interferometry. Kazuki Tamura[1], Ken-ya Hashimoto[2], and Shinpei Okawa[1], *[1]Hamamatsu University School of Medicine, [2]University of Electronic Science and Technology of China. k.tamura@hama-med.ac.jp*

The stiffness of tissue structures changes with inflammation and canceration. On a cellular scale, properties related to the elastic modulus also depend on the cell type and cycle. Scanning acoustic microscopy (SAM)

measured the acoustic impedance of cells without contamination because its configuration allows the measurement through a hermetically sealed cell culture dish.

Our group has proposed a fully optical-based mechanical property measurement, aiming to implement this function on a commercially available optical microscope. The measurement principle includes two steps: optical excitation and vibration measurement. In the excitation step, a pulsed laser focuses on a petri dish surface to generate photoacoustic waves from the petri dish. Some photoacoustic waves generated in the petri dish reflect off the boundary between the sample (such as cells) and the petri dish and propagate to the outside of the bottom of the petri dish. Waves that reach the outside of the bottom surface and surface vibration are measured using an optical interferometer. Thus, the surface vibration amplitude relates to the acoustic impedance contrast between the petri dish and the sample.

This presentation discusses experiments on generating photoacoustic waves on a 1 mm polystyrene petri dish and detecting waves propagating in the thickness direction. Vibration measurements with a self-made Sagnac interferometer (488 nm, continuous wave) were made using the optical path of an inverted optical microscope with a 20x objective lens. The excitation light (527 nm, nanosecond pulse) irradiated onto the polystyrene plate, such as the opposite of vibration measurement.

Vibrations were measured at 0.40 μs and 1.19 μs related to direct propagation and multiple reflections. This experiment showed that photoacoustic waves could be measured using an optical microscope and completed the preparation for optically measuring the acoustic impedance.

6.5. Comparison of photoacoustic-based PAtrace biodistribution assessment with independent validation.

Cayla Wood[1], Sangheon Han[1], Riley Watson[1], Dmitry Nevozhay[1], Jennifer Meyer[1], Jason Cook[2], Amit Roy[2], Julie-Anne Burdick[2], Konstantin Sokolov[1], Richard Bouchard[1], *[1]Department of Imaging Physics, The University of Texas MD Anderson Cancer Center, Houston, TX, [2]NanoHybrids, Inc., Austin, TX, cawood@mdanderson.org*

Background: Many cancer subtypes do not respond to standard therapeutic techniques, implying the need for real-time, noninvasive imaging to monitor therapy response and quickly direct non-responders to an alternative treatment plan. We previously demonstrated use of photoacoustic (PA) imaging to quantitatively assess in vivo accumulation of a FR-targeted PA contrast agent, PAtrace, in a preclinical ovarian cancer model1. However, there is a need to further assess biodistribution of PAtrace to identify target organs and anticipate potential safety and efficacy concerns.

Methods: Nine wild-type athymic nu/nu mice were first imaged on the MSOT inVision 256-TF PA imaging system. Multi-wavelength volumetric PA imaging was performed pre-injection, mice were injected with EGFR-targeted PAtrace, and PA imaging was repeated for 30 min post-injection. Fluence-corrected images were unmixed for oxy-/deoxyhemoglobin and PAtrace within ROIs in the liver, spleen, and kidneys. To semi-quantitatively assess PAtrace accumulation postmortem, three mice were processed for Xerra cryo-fluorescence tomography, while another three were processed for UV-Vis spectrophotometry. The final three mice underwent PA imaging for 6 days post-injection, then were processed for Xerra.

Results: PAtrace PA values 30 min post-injection were consistent across mice, averaging 303.6±94.9 (liver), 28.1±15.0 (spleen), and 1.0±0.9 (kidneys). UV-Vis assessment yielded comparable results among organs, with normalized PAtrace concentrations of 16.7±9.6, 18.2±8.5, and 8.3±7.3 ng/mg in liver, gallbladder, and spleen, respectively. There was no measurable UV-Vis signal from kidneys. PA-based SO2 was similarly consistent across mice/organs, averaging 58.1±4.4%. 3 days post-injection, PAtrace PA values reduced significantly, by 76% and 63% in liver and spleen, respectively. After injection, Xerra fluorescence values averaged 31.6±8.8 (liver), 202.4±74.8 (gallbladder), and 6.5±2.6 (spleen), but decreased by 91% and 98% in the liver and gallbladder, respectively, 6 days post-injection, implying substantial hepatic clearance of PAtrace.

Conclusions: High PAtrace signals in the liver, gallbladder, and spleen, assessed with PA, UV-Vis, and Xerra, imply that PAtrace is taken up and cleared entirely by the hepatic system, which is consistent with previously demonstrated liposomal clearance dynamics. Further studies will continue to evaluate PAtrace biodistribution and safety for future clinical translation.

[1]C. Wood et al. Clinically translatable quantitative molecular photoacoustic imaging with liposome-encapsulated ICG J-aggregates. Nat Commun 12, 5410 (2021).

6.6. Eavesdropping the tissues in action with high-speed photoacoustic microscopy. Junjie Yao, *Department of Biomedical Engineering, Duke University, Durham, NC, USA, 27708, junjie.yao@duke.edu*

Acoustically detecting the optical absorption contrast, photoacoustic microscopy (PAM) has become an enabling tool in biomedical studies, with its high spatial resolution, intrinsic sensitivity to functional information, and relatively deep penetration in tissues. In recent years, enabled by the innovative imaging mechanisms, scanning technologies, and the resultant high imaging throughput, it has become feasible to implement high-speed PAM to image otherwise challenging targets that are sensitive to dynamic changes and/or prone to motion artifacts, such as whole brain functions of small animals in response to pathological challenges. Moreover, various miniaturized high-speed PAM systems have been developed for handheld, wearable, and even head-mounted applications, enabling the study of highly dynamic physiologic and pathophysiologic processes, such as longitudinal monitoring of rare circulating tumor cells of melanoma patients. All these technical innovations have allowed the acceleration of PAM systems without sacrificing the imaging performance, and broadened their applications in life sciences.

7. Quantitative Ultrasound Models Session

7.1. Effects of cylindrical-Gaussian form factor for quantitative collagen fiber characteristics assessment in myopic guinea pig eye sclera. Kazuyo Ito[1], Quan V. Hoang[2,3,4], Cameron Hoerig[5], Sally A. McFadden[6], Jonathan Mamou[5], *[1]Institute of Engineering, Tokyo University of Agriculture and Technology, [2]Singapore Eye Research Institute, Singapore National Eye Centre, Duke-NUS Medical School, Singapore, [3]Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, [4]Department of Ophthalmology, Columbia University Irving Medical Center, New York, NY 10032, USA, [5]Department of Radiology, Weill Cornell Medicine, [6]Vision Sciences, School of Psychological Sciences, College of Engineering, Science and Environment, University of Newcastle, NSW, Australia*

As myopia progresses, excessive eye elongation alters collagen fibers microstructural properties within the eye wall (sclera). High-frequency quantitative ultrasound (QUS) can quantify collagen changes non-invasively. In a previous study, QUS parameters were obtained by applying a spherical Gaussian scattering model. However, this model did not appropriately model the elongated collagen fiber geometry. This study introduces the cylindrical-Gaussian model for the QUS parameter analysis to characterize the collagen-rich scleral tissue in myopic guinea pig (GP) eyes.

Form-deprivation myopia was induced in GPs by plastic diffusers over the right eye from 6 days of age for 1, 2 or 3 weeks (n = 5, 9 and 4 GPs respectively). Untreated left eyes were used as controls. Enucleated eyes were raster scanned using an 80-MHz transducer to acquire 3D radio-frequency (RF) data. The transducer had a focal length of 2.2 mm, f-number of 2, and a -6-dB bandwidth extending from 41 to 109 MHz. Effective scatterer diameter (ESDc) and effective acoustic concentration (EACc) were obtained by applying a cylindrical-Gaussian scattering model to the data. For comparison, ESDs and EACs were also obtained using a spherical-Gaussian scattering model. To evaluate myopia effects on QUS parameters, statistical tests were performed (i.e., Kruskal-Wallis tests).

The cylindrical-Gaussian scattering model showed significant lower root-mean-square-error. The inter-ocular differences (i.e. Myopic right eyes – Fellow control left eyes) in ESDc estimated by cylindrical-Gaussian FF showed a significant difference between the 2-weeks versus 3-weeks of myopia inducement group. The Cylindrical-Gaussian model is more biologically reasonable for the application to the fiber-rich structure, and could be a valuable alternative for the assessment of the changes in the scleral collagen fiber in myopic eyes.

7.2. Comparison of different methods to measure and model ultrasonic attenuation in cortical bone. Brett Austin McCandless[1], Kay Raum[2], Marie Muller[1]. *[1]Department of Mechanical and Aerospace Engineering, NC*

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The assessment of bone microstructure and bone mineral density (BMD) is important in screening for various bone diseases, such as osteopenia and osteoporosis. Dual x-ray absorptiometry (DXA) is the most commonly used technique for evaluating BMD; however, alternatives are necessary due to the use of ionizing radiation and low resolution, the latter of which prevents obtaining information on bone microstructure. Quantitative ultrasound (QUS) presents a potentially attractive alternative. The microstructure of porous media, such as cortical bone, influences the attenuation of ultrasound; as such, ultrasound attenuation can be used to obtain information about the microstructure of cortical bone. Different models and measurement methods may be used to estimate ultrasonic attenuation in cortical bone. In this study, three different methods of measuring ultrasonic attenuation were used. 2D finite-difference time-domain simulations were conducted in 12 different maps mimicking cortical bone. These maps were four millimeters in the direction of propagation. The pore densities and pore size distributions in the bone matrix, as well as the absorptive properties of the bone and porous matrices, were specified for all simulations (pore diameter ranging from 30 to 100 µm, pore density ranging from 3 to 5% area fraction, absorption ranging from 0 to 42 dB/cm at 6 MHz). Attenuation was measured within the pulse bandwidth as a function of frequency using the independent scattering approximation (ISA), a cortical backscatter method (CortBS), and the reflections from the two surfaces of the cortical bone map. An excellent agreement was found between the three methods for moderate levels of absorption around 6 MHz. For higher frequencies, the ISA approximation becomes less applicable, probably due to a change in scattering regime.

7.3. Accurate simulation of acoustic wave propagation for quantitative ultrasound applications. Karthik J. Nagabhushana[1], Aiguo Han[2], *[1]Texas Instruments, [2]Department of Biomedical Engineering and Mechanics, Virginia Tech, aiguohan@vt.edu*

Quantitative ultrasound (QUS) techniques have promising applications in disease diagnosis. Accurate simulation of ultrasonic wave propagation can significantly benefit the development and refinement of QUS techniques. For instance, ultrasonic backscatter signals can be predicted from histological slides if simulations can be performed accurately. The k-Wave toolbox has been widely used in many simulation applications. However, its accuracy in QUS simulations has not been fully documented. This study 1) assesses the accuracy of the acoustic backscatter versus frequency simulated by k-Wave and 2) proposes a strategy to improve accuracy.

Scattering from fluid spheres was simulated using k-Wave (1-3.5 MHz). Results were compared with 1) exact solutions from acoustic scattering theory (used as the reference), 2) numerical solutions from the spatial Fourier transform of the medium, and 3) simulation results from Field II. The influences of spatial resolution and impedance contrast on simulation accuracy were studied. Three simulation setups were studied to evaluate practical considerations, such as the imperfect plane wave created by a focused transducer and the effects of near-field and far-field observations. A strategy based on rediscretizing the medium was proposed to improve the simulation accuracy for a given spatial resolution and to reduce the required spatial resolution for a given accuracy target.

At a spatial resolution of 25 µm, the k-Wave-simulated backscatter spectrum from a 1-mm sphere had a root mean square error (RMSE) of 3.4% of the peak value in the far-field plane wave setup, more accurate than the Fourier transform or Field II results. The RMSE increased to 90.1% at a spatial resolution of 100 µm. However, applying the proposed strategy reduced the RMSE to 10.8% at 100-µm resolution. Similar trends were observed for simulations with multiple spheres. This work demonstrated the performance of k-Wave simulation for QUS applications and provided an effective strategy to improve accuracy. [Supported by NIH R01CA226528 and R21EB032638]

7.4. Addressing assumptions in describing the cervical extracellular matrix through ultrasound speckle. Alexandra Christensen[a], Amber Possell[a,b], Ivan Rosado-Mendez[a,b], and Timothy J. Hall[a], *[a]Medical Physics*

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Purpose: Ultrasound speckle statistics can describe various types of sub-resolution scatterers, enabling quantitative tissue characterization in complex, dynamic tissues like the cervix. However, speckle statistics assume sample independence, which is not upheld in raw ultrasound signals and may affect estimate bias and variance. This study aims to explore microstructural changes throughout pregnancy in the rhesus macaque cervix using speckle statistics and to test the validity of this assumption.

Methods: Cervix scans from a longitudinal study of 14 rhesus macaques throughout pregnancy were investigated. To examine the effects of correlation in echo envelope samples, speckle statistics were calculated both with the full dataset and with a dataset subsampled by axial and lateral correlation lengths for comparison. Estimates from envelope amplitude include the Nakagami parameter and coefficient of determination (R2) of the Nakagami parameter as a function of gestational age.

Results: The median Nakagami parameter across all subjects was summarized in 5mm square ROIs in the central anterior cervix. In the de-correlated case, the Nakagami parameter increased from 0.41 (IQR 0.16) to 0.51 (IQR 0.07) between the 4th and 23rd (last) week of pregnancy. The mean R2 value was 0.79±0.003 over all timepoints. Without accounting for sample correlation, the Nakagami parameter increased from 0.39 (IQR 0.11) to 0.5 (IQR 0.6), and the mean R2 was 0.85±0.02.

Discussion: These results are an encouraging step toward characterization of the cervix using speckle statistics. The increase in the Nakagami m indicates microstructural disorganization as pregnancy progresses. It is also apparent that sample independence is not a significant concern for speckle statistics in this dataset. Future work will continue to refine methods for increased sensitivity and apply them to human cervix scans.

Wednesday Morning June 7th

8. Devices Session

8.1. An electronic radiological clip having ultrasound identification for localization of lesions being treated by neoadjuvant chemotherapy. Jenna Cario, Michael L. Oelze, ECE, *University of Illinois Urbana-Champaign (UIUC), Beckman Institute for Advanced Science and Technology, UIUC, jcario2@illinois.edu*

During the treatment of breast cancer via neoadjuvant chemotherapy (NAC), radiological clips are used to track lesions. Marking lesions allows them to be located and distinguished from their surroundings post-NAC, but morphological changes to the treated regions due to NAC can affect the visibility of marking clips in ultrasound, sometimes to a degree which requires the use of alternative, less comfortable modalities to visualize the clips in preparation for procedures such as surgical resection or biopsy. We propose an electronic clip design leveraging active communication with an ultrasound imaging probe, improving visibility and differentiation of clips in ultrasound. The device design uses pseudo-noise (PN) codes as the ultrasonic identification signals transmitted to improve localization, and a Verasonics imaging system has had supplemental processing routines added to allow multiple clips to be active and distinguishable in the imaging field in real time.

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8.2. Volumetric tracking of beacon signal during vascular access: system design and optimization. Jintan Zhang, Emad M. Boctor, Jeeun Kang, *Johns Hopkins University, Baltimore, MD 21218, eboctor@jhu.edu, kangj@jhu.edu*

Vascular access is the most common medical procedure in the world, with over a billion insertions performed annually. However, locating and navigating the cannula tip through various layers of human tissues is challenging with conventional ultrasound (US) imaging due to inherently small size of the cannula, the complicated tissue and vessel interactions with the cannula, and often requires several painful and time-consuming attempts at insertion depending on the experience level of the clinician. Furthermore, there is a

high rate of early failure that can lead to complications, including extravasation, thrombophlebitis, and compartment syndrome, as well as delays in delivery of therapeutic medications. To alleviate patients' pain and safer and reliable vascular access procedures, we design a novel guidance system that accurately tracks the spatial location of active contrast generated from the cannula, in which wide field of view (FOV) and tracking accuracy can be both acquired. The transmitter component should be equipped within the insertion tool. The active beacon pulse generated will be captured by the receiver component while passing through the patient's body. A custom bracket, attached to the clinical US imaging array, will have multiple receive sensors on its contour contacting tissue surface. In this abstract, we tested various scenario of having different number and distribution of receive sensors (>3), signal to noise ratio (SNR, 0-10 dB), and guidance depth up to 4 cm. Encouragingly, the simulated bracket system with three tracking elements provided sub-millimeter tracking accuracy at 4-cm depth when the SNR is higher than 6 dB, which is easily achievable in soft tissue (i.e., {0.12±0.02, 0.16±0.03, 0.14±0.03, 0.17±0.04, 4.46±12.01, 19.56±12.90} mm at SNR of {10, 8, 6, 4, 2, 0} dB, respectively). Therefore, the bracket system will enable a volumetric tracking of tool with beacon pulsing from deep tissue.

8.3. Wearable Ultrasound System for Controlling Upper-limb Prosthetics. Afsana Hossain Rima[1,2], Zahra Taghizadeh[1], Abhishek Aher[1], Ahmed Bashatah[1], Siddhartha Sikdar[1,3], *[1]Department of Bioengineering, George Mason University, Fairfax, VA, [2]Department of Electrical and Computer Engineering, George Mason University, Fairfax, VA, [3]Center for Adaptive Systems of Brain-Body Interactions, George Mason University, Fairfax, VA*

Background: Sonomyography (SMG), an emerging modality that uses ultrasound to detect muscle deformation, has been gaining interest as a viable alternative to surface electromyography (sEMG) for detecting real-time functional activity of muscles and generating control signals to actuate external devices like prosthetic hands. In this study, we present a 4-channel ultrasound system with miniaturized electronics optimized for upper limb prosthetic control. We used frequency-modulated continuous wave imaging instead of traditional pulse-echo to simplify the electronics and captured 4-channel M-mode images of the muscle interfaces from human subjects. We also evaluate the potential of using 1-3 piezocomposite transducers over PZT transducers for capturing higher quality M-mode images from the forearm muscle activity.

Method: The study utilized a unique front-end instrumentation along with a wearable ultrasound system with four 1-3 piezocomposite transducers for reconstructing ultrasonic scan lines from frequency modulated continuous wave signals. A key feature of using 1-3 piezocomposite transducer over PZT transducer is the reduction of acoustical mismatch between tissue and the transducer, which reduces the energy losses and signal attenuation at the site of transmission of ultrasound signal.

Result: This study demonstrates the ability to use a 4-channel ultrasound image acquisition system to capture muscle interfaces of the forearm and classify five grasps with >97% classification accuracy. We have computed and compared the bandwidth and signal-to-noise ratio from the frequency domain data captured by PZT vs 1-3 piezocomposite transducers. The study showed that 1-3 piezocomposite has wider bandwidth and improved signal-to-noise ratio compared to PZT, and that 1-3 piezocomposite transducers can provide higher-resolution ultrasound images for controlling upper-limb prosthetics.

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8.4. Wearable ultrasound-integrated AR navigation system for lumbar puncture guidance. Baichuan Jiang[1], Liam Wang[1], Keshuai Xu[1], Martin Hossbach[2], Alican Demir[2], Purnima Rajan[2], Russell Taylor[1], Ahbay Moghekar[3], Pezhman Foroughi[2], Peter Kazanzides[1] and Emad Boctor[1]. *[1]Department of Computer Science, Johns Hopkins University. [2]Clear Guide Medical Inc. [3]Department of Neurology, The Johns Hopkins Medical Institute. eboctor@jhu.edu*

As one of the most commonly performed spinal interventions in routine clinical practice, lumbar punctures are usually done with only hand palpation and trial-and-error. Failures can prolong procedure time and

introduce complications such as cerebrospinal fluid leaks and headaches. Therefore, an effective needle insertion guidance method is desired.

In this work, we present a complete lumbar puncture guidance system including a wearable "patch"-like ultrasound imaging device, volume-reconstruction and bone surface estimation algorithms and two alternative augmented reality (AR) user interfaces (UI) for needle guidance: both a HoloLens-based and a tablet-based solution.

We conducted a quantitative evaluation of the end-to-end navigation accuracy of both solutions, which shows that our system can achieve an overall accuracy of 2.83mm and 2.76mm for the Tablet-based and the HoloLens-based navigation interfaces, respectively. In addition, we conducted a preliminary user study to qualitatively evaluate the effectiveness and ergonomics of our system on lumbar phantoms. The results show that users were able to successfully reach the target in phantoms in an average of 1.12 and 1.14 needle insertion attempts for Tablet-based and HoloLens-based systems, respectively.

Overall, the proposed lumbar-puncture guidance system has demonstrated sufficient navigation accuracy via validation experiments and promising usability via a user study, thus exhibiting the potential to reduce the failure rates of LP procedures.

8.5. Automated radiological bead detection in breast tumors for calibrating quantitative ultrasound. Yuning Zhao, Michael L. Oelze, *ECE, University of Illinois Urbana-Champaign (UIUC), Beckman Institute for Advanced Science and Technology, UIUC, yuningz4@illinois.edu*

Quantitative Ultrasound (QUS) is a promising imaging method for detecting response of breast cancer to neoadjuvant chemotherapy. QUS is sensitive to tumor cell death, which is a hallmark of response. However, traditional QUS calibration methods using external reference materials are limited by attenuation and transmission losses in vivo and require additional scans. To address these issues, we used an in-situ calibration target, i.e., a 2-mm diameter titanium bead, to obtain a reference signal.

Automated bead detection is crucial to improve the efficiency of QUS calibration. However, detecting bead signals in tumor images is challenging due to the presence of strong scatterer signals within the tissue. Separating the target bead signals from these strong scatterer signals by intensity alone can be difficult. To solve this problem, we employed a cross-correlation method to distinguish the bead signal from other similar signals in tumors with embedded beads and locate the bead. The method successfully located the bead signal with 95% accuracy in B-mode images of breast tumors. This automated approach has the potential to improve the efficiency and accuracy of QUS calibration for breast cancer imaging.

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9. Funding Opportunities Session

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