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***In vivo* Lag-one Coherence Measurements Using Matrix Arrays**

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Objectives: Diffuse reverberation is a significant source of image degradation in abdominal ultrasound. Clutter induced by reverberation is often considered to be spatially incoherent. The nearest element correlation of backscatter signals provides a robust measure of such incoherent clutter [1]. We recently presented Lag-one Spatial Coherence Adaptive Normalization (LoSCAN) [2], an image formation technique that adaptively compensates for the SNR loss due to incoherent clutter. Here, we present *in vivo* LoSCAN images obtained with a 1024-element matrix array and explore the benefits of 2D clutter reduction.

Methods: We developed a 2D LoSCAN framework applicable to matrix arrays. We validated this framework using Field II-simulated cyst phantoms of varying native contrasts and channel SNR, with a modeled 64x64 symmetric 2D array. Using these simulated data, we studied the impact of partially correlated noise (PCN) with controlled spatial correlation lengths (1λ to 3λ). Sub-aperture beamforming and a short-lag version of LoSCAN were explored as strategies to circumvent the PCN-induced contrast loss. We also acquired experimental data using a custom 64x16 2D array connected to a 1024-channel Verasonics system. We acquired fundamental and harmonic channel data from the liver of two healthy volunteers and performed 2D spatial coherence-based clutter analysis.

Results: Compared to B-mode imaging, matrix LoSCAN preserved the native contrast and improved the lesion detectability, measured with the generalized contrast-to-noise ratio (gCNR), over a wider range of channel SNR. *In vivo* observations demonstrated the anisotropy of reverberation-noise correlation length. Matrix LoSCAN also improved the gCNR of abdominal anechoic targets from 0.92 to 0.97 in fundamental images and from 0.91 to 0.97 in harmonic images.

Conclusions: Matrix LoSCAN effectively suppressed the incoherent clutter in abdominal ultrasound images. *In vivo* examples demonstrated the advantages of multi-dimensional clutter analysis.

[1] Long *et al.*, IEEE-TUFFC, 2018

[2] Long *et al.*, IEEE-TUFFC, 2020

***In vivo* Murine Cardiac Strain Imaging with Adaptive Bayesian Regularization**

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Objectives: Murine cardiovascular disease models play a critical role in understanding cardiovascular disease progression and therapy development. Cardiac strain imaging (CSI) is an ultrasound radio-frequency (RF) signal-based method to estimate myocardial tissue elasticity. Here, we report on a murine CSI framework incorporating adaptive Bayesian regularization in a longitudinal study of myocardial remodeling associated with myocardial infarction (MI) and ischemia-reperfusion (IR) models.

Methods: RF data from three male BALB/CJ mice (one MI, one IR and one sham) were collected at pre-surgery (BL) and 1,2,7 and 14 days post-surgery using MS 550 D transducer (fc = 30 MHz) at 235 fps in the parasternal long axis view (Vevo 2100, Fujifilm Visualsonics). MI was induced by ligation of the left anterior descending coronary artery (LAD) via thoracotomy. For IR, the tie was released after 45 minutes of ischemia. Interframe displacements were estimated using a three-level block matching algorithm with adaptive Bayesian regularization. Lagrangian cardiac strain tensor was derived by segmenting myocardial wall starting at the EKG R-wave and accumulating incremental deformations over a cardiac cycle. Segmental peak radial (Er) and longitudinal (El) strains were derived. Regions with fibrosis were confirmed using Masson's trichrome staining.

Results: No significant variation in strain was observed for sham mice. Apical infarcts were identified in both MI and IR mice either by marked reduction in segmental strains or sign reversal of strain when compared to BL imaging. Anterior apical segment peak Er at BL, Day 14 for sham =16.52%, 38.82%; MI =38.29%, 10.74%; IR = 20.76%, 8.81%. Strain variations were associated with increased collagen content in the infarcted regions (as seen in slide interpretation).

Conclusion: Our results show that our proposed framework provides high quality strain images with ability to distinguish between infarcted and viable regions in murine models of MI and IR demonstrating the potential for early detection of cardiac dysfunction.

Combining Variance of Acceleration and Vector Flow Imaging of Human Cadaveric Carotid Plaques

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Background: Carotid atherosclerotic plaque composition and wall shear stress convey susceptibility to rupture, a precursor to ischemic stroke. Variance of acceleration (VoA) imaging, which assesses plaque composition, and vector flow Doppler, used to estimated wall shear stress (WSS), are herein combined and applied to evaluating human carotid plaques with varying geometries.

Method: Excised human carotids from four recently deceased males and females aged 63-83 years were attached to a custom flow setup and pressurized to ~80 mmHg or ~120 mmHg while circulating whole milk at 300 or 600 ml/min. Custom beam sequences integrating focused- or plane wave-derived VoA and vector flow with or without angle compounding were executed using a Verasonics scanner and L7-4 transducer. From the acquired raw data, 2D vector flow, wall shear stress, and VoA were computed, with spatially matched histological validation of VoA outcomes.

Results and Conclusion: WSS on all four examined plaques increased with flow rate. At 600 ml/min flow, the peak WSS on the most stenotic (>50%) plaque, which was highly calcified, was 4.16 Pa versus an average peak WSS of 2.13±0.30 Pa over the three other plaques (each <50% stenotic and not highly calcified). Focused- and plane wave-derived VoA yielded comparable delineations of calcium, collagen, and lipid regions, which correlated well with matched histology. Results suggest that high framerate VoA imaging may be combined with vector flow techniques to visualize plaque morphology and detect heightened WSS associated with stenosis. Future studies will incorporate fluid structure interaction modeling to validate WSS estimates.

A Miniaturized Time Delay Spectrometry Based Wearable Ultrasound Imaging System

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Background and Aims: With the increased adoption of miniaturized point of care commercial ultrasound systems available in the market, in recent years, wearable ultrasound imaging systems have been gaining attention. These systems have the potential to push the frontier of ultrasound from diagnostic imaging applications to biosignal sensing and monitoring applications. Research on this topic has primarily focused on transducer design, and the signaling and instrumentation has not received much attention. We have developed a novel imaging method for wearable ultrasound systems based on time-delay spectrometry (TDS) that employs a low-voltage, wideband, chirp transmit signal to establish a relationship between time of flight of the signal and transmit frequency. TDS can enable significantly simplified instrumentation compared to conventional pulse-echo imaging with high voltage and short duration transmit pulses along with electronics that operate in the MHz frequency range. In previous years, we have shown benchtop implementations of a TDS system that can be used with commercial single element transducers. We also showed the acoustic output parameters for the TDS system to establish its safety for imaging purposes and demonstrated the ability to dynamically image deep-seated tissue in real-time. We will show a fully miniaturized system with a microprocessor, quantify power consumption and show tissue M-modes from that system.

Methods: The prototype TDS system consists of a power conditioning sub system, a chirp subsystem, an analog TDS subsystem, a TI C2000 DSP microprocessor, and a commercial 4.25 MHz single element PZT. The power subsystem converts a dual cell 7.4V LiPo battery to ±5V to power analog circuitry and +3.3V for the chirp subsystem. The chirp subsystem consists of an AD5930 swept-frequency source (100 kHz/ms) that is programmed by the microprocessor. The TDS subsystem contains a custom RF transmit amplifier to boost the chirp signal, a demodulator for TDS mixing, and a receive amplifier and low-pass filter. The resulting downmixed signal is digitized and processed using FFT on microprocessor which was powered by a standalone supply. The power measurements were collected using a JouleScope power meter attached at the battery, then at the output of the power subsystem, and finally at the microprocessor power input to measure overall power consumption and the consumption at the different subsystems.

Results: The power consumption of the chirp was 40mW for all four channels. The TDS analog subsystems were 602mW for all four channels. At the battery, the power consumption was 1.92W. Additionally, the power consumption of the processor performing digitization, FFT and sending the data to a host computer via RS232 was 576mW. The system was powered by a 7.4V 2000mAh battery and it can scan for 7 hours. With these TDS drive parameters, we obtained in-vivo, M-mode images with average successfully tracked muscle-tissue boundaries in vivo in humans for imaging depth up to 5 cm.

Conclusion: We demonstrate the ability of a miniaturized time delay spectrometry-based ultrasound imaging systems for in-vivo ultrasound imaging. Having shown the power requirements, we believe the system can be used for wearable applications. Future work on optimizing the power and signal processing of the system can provide us with longer scan time per battery charge.

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Real-time registration and display of 3D echocardiography and 3D interventional device reconstructions from x-ray fluoroscopy

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Background: Valvular interventions rely on accurate visualization of catheter-based devices as they are navigated through three-dimensional cardiac chambers and vessels. A real-time, 3D fusion platform was developed for display of 3D device reconstructions derived from x-ray fluoroscopy relative to anatomy portrayed in transthoracic echocardiography (TTE). This work presents an evaluation of the fusion platform using a custom-made phantom simulating multi-modality imaging conditions for interventions such as transcatheter aortic valve replacement (TAVR).

Methods: A software and hardware framework generates a real-time 3D display of valve reconstructions relative to volumetric TTE with two concurrent device tracking tasks. Task one determines the 3D pose and shape of a TAVR valve device from biplane (2-view) fluoroscopy images. Task two registers volumetric TTE to x-ray coordinate space by tracking the 3D pose of a rigid fiducial attachment to the probe based on its appearance in 2D monoplane fluoroscopy. Platform execution time and TTE-to-x-ray registration error were evaluated with a multi-modality thoracic phantom containing a tissue-mimicking slurry and interchangeable imaging inserts. Platform processing speed (fps) was measured while imaging an insert with simulated cardiac cavities and an expanding TAVR valve device. Registration error was measured with a second insert embedded with x-ray and ultrasound-visible targets, by comparing the positions of corresponding targets upon registration of TTE to x-ray coordinates. Based on prior literature on cardiac interventional image guidance, the goal was to achieve registration errors under 5 mm.

Results: Platform frame rates measured under conditions of probe and valve motion ranged between 6.6 – 7.8 fps. Target Registration Error of TTE-to-x-ray registration was measured with the probe in four standard acoustic windows. Average errors ranged from 1.12 – 1.61 mm (95th percentile ≤ 1.77 mm). *Conclusion*: A 3D TTE/X-ray fusion platform has been developed to provide real-time displays of device/anatomy interrelationships and aid device navigation during valvular interventions.

Acoustic signal injection for reverse engineering of image formation Isaac Brighton1, Nick Bottenus1

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Objective: To demonstrate the use of a controlled acoustic source to study the image formation process of a black-box ultrasound system.

Methods: We use a single element transducer as a switchable acoustic point source, controlled by a microcontroller through a pulser. This source injects its acoustic signal into the imaging field where it is received by an ultrasound scanner and processed as though it were a pulse-echo signal from that system. First, we demonstrate the use of this technique with synchronization to imaging sequences on a research scanner. The acoustic source, active only during a single pulse echo event per frame, creates distinctive patterns depending on how each transmission is processed into part of the image. Second, we demonstrate this technique with a black-box system (without a synchronization signal) using manual pulse timing. Moving the switchable source through time and space relative to the imaging sequence provides insight to the receive processing of each transmission to uniquely identify common beamforming strategies.

Results: We identify spatial patterns observed on the scanner display indicative of dynamic receive, virtual source synthetic aperture and REFoCUS beamforming. These approaches cannot ordinarily be distinguished based on the transmit beam pattern or pulse sequence. The injected signal reveals spatial masks and focal delays applied to the received signal. In the case of REFoCUS, a distinctive multi-lobed pattern is formed when the signal is injected off-axis from a transmit beam. We also study patterns observed with plane wave imaging.

Conclusion: While the transmissions of an imaging sequence can be observed using a receiving element, acoustic signal injection provides an opportunity to probe the receive processing and image formation process. This technique could be useful for investigating the sensitivity of synthetic aperture imaging to target motion and as a tool for preventing the infringement of patented image formation methods.

Real-Time Reverberation Reduction of Ultrasound Channel Data Using a 3D Convolutional Neural Network

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Background, Motivation and Objective Diffuse reverberation is caused by multiple reflections of a wavefront before returning to the transducer. This noise degrades both B-mode image quality and ultrasound channel signals, which decreases the performance of techniques that rely on channel signals. Previously, we implemented a 3D convolutional neural network (3DCNN) to remove reverberation noise from the channel signals prior to beamforming [1]. In this work, we investigate architecture changes to this 3DCNN to allow reverberation noise reduction of ultrasound images in real-time.

Statement of Contribution/Methods The 3DCNNs were trained using the same approach as in our previous work [1]. To increase network speed, adjustments to the network architecture such as decreasing the convolution kernel size, decreasing the number of layers, combining the real and imaginary layers, and reducing the network to a series of permuted 2D convolutions were investigated. The trained networks were used in conjunction with a GPU software beamformer on a Verasonics Vantage 256 scanner and L12-3v transducer. A coherent plane wave compounding transmit sequence was used with 128 plane waves over an angular span of 30. The frame rate (fps) was measured to be the rate at which the received data was time-delayed, filtered, and displayed as a B-mode image. The previous network [1] and the new network variations were tested for speed and performance of reverberation reduction.

Results/Discussion Images of the real-time networks applied to in-vivo data of carotid artery and benign thyroid cysts are shown below for the original unfiltered data (a), the 3DCNN from [1] (b), and one of the new network architectures (c). The frame rates for the networks are given, along with the GCNR, LOC and contrast of the ROIs shown in (a) for the networks in the Table. The original network yielded 11 fps, while the new network architecture modifications ranged from 15 to 30 fps. Many of the new architectures yielded similar performance to the original network. However, a performance tradeoff was observed for the faster, more simple networks. Original Network from [1] fps: 11 Simplified Network fps: 15

[1] Brickson LL, Hyun D, Jakovljevic M, Dahl JJ. Reverberation Noise Suppression in Ultrasound Channel Signals Using a 3D Fully Convolutional Neural Network. IEEE Trans Med Imaging. 2021

Recondensation of vaporized nano-sized phase-change contrast agents for rapid, flow-independent ultrasound localization microscopy

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Background: Super-resolution imaging with ultrasound localization microscopy (ULM) is a promising technique to surpass the diffraction limits of traditional ultrasound imaging. ULM is based on the buildup of millions of subwavelength localizations of gas-filled ultrasound contrast agents (UCAs) as they flow through the vascular space. The efficacy of this technique is limited in regions of slow flow due to reduced localization rates and diminished isolation of microbubble signal from tissue. This work leverages the unique spatiotemporal dynamics of phase-change contrast agents (PCCAs) to address these limitations. PCCAs are superheated perfluorocarbon droplets that can be vaporized into bubbles on demand with ultrasound pulses to enable spatiotemporal control of bubble formation.

Methods: A 16-MHz linear array connected to a Verasonics research ultrasound system was used to capture high-frame rate acquisitions (0.1 sec., 1000 Hz) of contrast agents flowing through an *in-vitro* flow phantom. The 2D interframe correlation coefficient and bubble localization rate of PCCAs was compared to UCAs under flow (~1 mm/s) and no flow conditions.

Results: Nano-sized PCCAs have an inherent low interframe correlation at all flow conditions due to rapid recondensation of PCCAs between ultrasound pulses, while the interframe correlation of UCAs remained high due to limited movement at low flow speeds. This led to a higher bubble localization rate for PCCAs, since a new population of bubbles was localized with each ultrasound pulse. The localization rate of UCAs increased with the flow rate, but remained significantly lower than PCCAs.

Conclusions: The on and off nature of PCCA vaporization/recondensation events produces a contrast signal that can be separated from tissue regardless of flow conditions. This also allows for rapid ULM at low flow speeds, where UCAs require long acquisition times for adequate microbubble movement and localization rates. This work was supported by NIH grant R21 HD097485.

Ultrafast Transmit Approaches for High Frequency Ultrasound Applications

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Background: Recent advances in the availability and capabilities of open platform ultrasound systems has led to a significant increase in the development and scope of novel ultrasound imaging modalities, including super-resolution and ultrafast Doppler imaging. However, most open platforms currently available are primarily intended for use by the research community which can lead to difficulties in the translation into the preclinical/clinical domain. Support for true high-frequency ultrasound (>20 MHz) is also limited, with most systems requiring compromises to sampling rates or real-time imaging frame rates. We investigated the extension of clinical ultrafast transmit approaches to high-frequency transducers using the Vevo F2 (Fujifilm Visualsonics Inc., Toronto, Canada).

Methods: Ultrafast transmits were implemented on the Vevo F2 VADA architecture using the L38, UHF29x and UHF57x, with transmit frequencies of 6 MHz, 21 MHz, and 38 MHz respectively. Plane waves were generated in varying degree steps and ranges and the penetration, resolution and frame rate were compared using a tissue mimicking phantom with wire, hyper- and hypo-echoic inserts. Transmit cycles were varied to assess the penetration versus resolution trade-off.

Results: Matched imaging examples will be presented comparing system-processed B-mode imaging to the plane-wave pulse sequences post-processed in MatLab. Images will be assessed for penetration, resolution, frame rate and CNR (Contrast to Noise Resolution).

Parameter Optimization Using a Deep Neural Network for Multiparametric Ultrasound Imaging of Prostate Cancer

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Background: Conventional B-mode ultrasound, which is currently used to guide transrectal biopsy of the prostate, often lacks sensitivity for prostate cancer. Previous work has demonstrated the utility of multiparametric ultrasound (mpUS)—combining acoustic radiation force impulse (ARFI) imaging, shear wave elasticity imaging (SWEI), quantitative ultrasound midband fit (QUS-MF), and B-mode—for improving the contrast-to-noise ratio (CNR) of prostate cancer *in vivo*. (1) Previously, a linear combination of the four modalities was used to produce the 3-D mpUS volume, with linear weights determined by a support vector machine. In this work, we investigate the application of a deep neural network (DNN) to generate the mpUS volume, with the network's weights optimized to maximize CNR. *Methods:* In an ongoing IRB-approved study, co-registered 3-D ARFI, SWEI, QUS-MF, and Bmode prostate volume data have been obtained in subjects prior to radical prostatectomy, using the Siemens SC2000 scanner and the Siemens 12L4 or Acuson ER7B transducer. Cancerous and noncancerous regions of each prostate were manually segmented using cognitive registration with histology. A DNN with two hidden layers was used to transform the four input modalities at each voxel to a resultant mpUS value, with the loss function designed to maximize CNR in the training dataset.

Results: In an anatomical prostate phantom dataset, the DNN mpUS volume resulted in improved visualization of the prostate capsule boundary compared to the linear mpUS volume. The outputs of the hidden layers of the network provide additional modes of contrast and insight into the specific features emphasized by the neural network. The relative computational simplicity of the network, which consists primarily of matrix multiplication operations and activation functions, makes it feasible for generating mpUS prostate volumes in a clinical setting.

(1) Morris et al., *Ultrasound Med Biol*, 46(12): 3426–3439, 2020

Backscatter Coefficient for the Quantification of Liver Fat: A QIBA Perspective

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Conventional B-mode ultrasound is commonly used for detection of liver steatosis with parenchymal brightness as a major diagnostic criterion. With increased interest in non-alcoholic fatty liver disease (NAFLD), a quantitative and reproducible measure of backscatter is needed to reduce user subjectivity and system dependence and to complement attenuation and elastography parameters. The liver-to-kidney echo amplitude ratio has shown good sensitivity for identifying fat fraction exceeding 5% (considered the cutoff for healthy liver) and is available on some scanners. However, this hepatorenal index has limitations due to accessibility, renal backscatter anisotropy, scanner dependencies, and interpatient variability in kidney reflectivity. An index of backscatter distribution based on Nakagami parameters has also been implemented on clinical systems, but validation is scarce. For this QIBA profile, the backscatter coefficient (BSC), which is the differential scattering cross section per unit volume for a scattering angle of 180 degrees, is being assessed as a viable biomarker. The BSC is related to B-mode “brightness” and typically computed from RF signals. Analysis must account for beam intensity, attenuation, solid angle, coherence, system settings, and transducer beam diffraction. The BSC frequency-dependent behavior can be fitted to predictions of a tissue microstructure model. Based on a literature review, BSC of healthy livers fall within the range of 1-10 x10-4 /cm-sr in the clinical frequency range (2-6 MHz) with a frequency dependence of approximately f1.2. Moderate to severe fatty livers ranged from 30 to 100 x10-4 /cm-sr with similar frequency dependence. Using phantoms that mimic the magnitude of normal and fatty liver scattering at 4 MHz, the accuracy and reproducibility of the BSC will be compared across researcher implementations using data from various manufacturer’s scanners. The QIBA/PEQUS Backscatter Working Group hopes to standardize the application of a BSC parameter for subsequent use as a biomarker of fatty liver disease.

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Random matrix theory to quantify structural changes in lung parenchyma

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We investigate Random Matrix Theory (RMT) as a tool to distinguish edematous and fibrotic lungs from healthy control lung, in rodent models of pulmonary edema and fibrosis in-vivo, and in pig lungs ex-vivo. According to RMT, highly scattering structures lead to specific characteristics in the distribution of singular values of the Inter-element Response Matrix (IRM, full synthetic aperture). When multiple scattering dominates (healthy lung), the singular values of the IRM are distributed according to a quarter circle. On the contrary, in the single scattering regime, the distribution of singular values departs from a quarter circle, resembling a Hankel distribution. We propose to exploit this feature to quantify multiple scattering in the parenchyma. Two metrics are defined to describe the singular value distribution: the expected value *E*, which is the weighted average of all singular values, and λmax, the singular value with the highest probability. A 128-element linear transducer operating at 7.8 MHz and a Verasonics scanner were used to collect IRMs from 6 control rat lungs in-vivo, 6 edematous rat lungs in-vivo, 21 areas of healthy pig lungs and 27 areas of edematous pig lungs ex-vivo. Data collected from pig and rat lungs agree. Significant differences were observed between edematous and control regions of pig lungs for both *E* and λmax (respectively p=6e-7 and p=1e-9). Significant differences were observed between edematous and control rat lungs for *E* ($p<0.02$). However, λmax did not discriminate edematous and control rat lungs. *E* was also able to discriminate fibrotic lungs from edematous lungs in rats ($p<0.005$) but was not able to discriminate fibrotic lungs from control lungs. These preliminary results to show the potential of these two new metrics to quantify structural changes in the lung parenchyma. More rodent studies should be performed to confirm these results.

Challenges and strategies for the screening of meningitis in newborns using quantitative ultrasound imaging

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Bacterial meningitis is a lethal disease causing 165 newborn deaths every day. This aggressive infection leaves severe sequelae among 30% of survivors. The current strategy to improve its prognosis is an early diagnosis by means of a lumbar puncture, invasive and potentially harmful, followed by antibiotic treatment. Cranial ultrasonography through the anterior fontanel of neonates is proposed as a new non-invasive procedure for meningitis screening. It is based on the assessment of the leukocyte concentration in cerebrospinal fluid (CSF) which may be related to the presence of both viral or bacterial meningitis. High frequency ultrasound imaging can be used to detect and quantify the very low concentrations of leukocytes in liquid samples (5-20 cells/µl) needed to achieve an effective meningitis screening. Within this work, recent advances made to adapt the cell concentration assessment to an *in vivo* setting are presented. One of the main issues related to this technology is focused on the estimation of the absolute concentration of leukocytes, which should be a patient independent measurement. Three different image analysis methodologies have been studied to determine the leukocyte concentration in CSF: pattern recognition algorithms, envelope statistics models and artificial intelligence (A.I.) algorithms. By means of both ultrasound field simulations and experimental images acquired from in-vitro samples using a single-channel scanning ultrasound system working at 20MHz, the quantitative ultrasound techniques are compared and discussed. Conditions expected in an *in-vivo* setting: SNR variations because of the mechanical coupling achieved, different tissue attenuation of patients, size dispersion of cell populations, wide range (0-5000 cells/µl) of involved cell concentrations expected and acoustic noise produced by multiple reflections in tissues are taken into account.

Ultrasound Imaging and Tissue Characterization Symposium AIUM/QIBA PEQUS Round Table Discussion: Liver Fat Measurement Opportunities and Challenges

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BACKGROUND: Hepatic steatosis, associated with metabolic syndrome and cardiovascular risk, is becoming a preeminent cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma. Quantitative measures of liver fat may help screen at-risk patients and assess disease progression or therapy response. Ultrasound is widely available and cost-effective, however accurate and reproducible quantitative tools are needed. The American Institute of Ultrasound in Medicine (AIUM) launched the Liver Fat Quantification (LFQ) Task Force in 2019, partnering with the Quantitative Imaging Biomarker Alliance (QIBA) in creating a new biomarker committee for pulse-echo quantitative ultrasound (PEQUS), approved in 2020.

PURPOSE: To facilitate an inter-disciplinary discussion addressing the clinical needs and current challenges in ultrasound-based quantitative tools such as those for liver fat quantification, we propose a round table discussion with two moderators (abstract authors) and 3-4 panelists as the culmination of a series of sequential AIUM/QIBA PEQUS abstract presentations.

FORMAT: This round table will follow five associated presentations from PEQUS members: biomarker science; each of three biomarkers (attenuation, backscatter, sound speed); and challenges in phantom design and fabrication. These preceding abstracts will set the stage for an open discussion on PEQUS biomarkers for liver fat quantification. After a short introduction, moderators (abstract authors) will ask panelists (PEQUS biomarker representatives) prepared questions covering topics including:

1. Current challenges in commercial implementations and clinical validation;

2. Reporting correlation with liver fat: biomarker values vs fat-quantification metrics;

3. Biological confounders and limitations;

4. Clinical guidelines and references

Moderators will also present comments and pose questions submitted live by attendees. *GOAL*: To help attendees understand the urgent clinical need for non-invasive measures of liver fat, the current limitations and gaps in knowledge for the use of PEQUS biomarkers in this context, and ongoing and future initiatives to address these challenges.

Developing a Region of Interest Selection Method for Automated Implementation of the ALARA Principle in Fetal Ultrasound

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Objectives: FDA guidelines suggest that ultrasound exposure should follow the ALARA (As Low as Reasonably Achievable) principle. Adherence to this principle is largely user-dependent and several studies indicate that compliance is lacking. Therefore, our goal is to develop a rapid, automatic technique to achieve ALARA acoustic exposure during fetal ultrasound imaging. Previous work has proposed that monitoring an image quality metric called lag one coherence (LOC) as transmit voltage changes could be used to effectively implement the ALARA principle. However, the long calculation time needed to determine LOC for whole images at multiple voltage levels is unreasonable to perform in a clinical setting. Therefore, the automatic identification of small image regions on which to perform the LOC calculation is important prior to broad implementation of an automated ALARA tool.

Methods: An algorithm for automated identification of viable regions to use for optimization was developed and tested on 150 B-mode images of fetuses and placentae. Clinical data used were collected at the Duke Fetal Diagnostic Center following an IRB-approved protocol. The images were split into 0.5 cm (axial) x 5 lines (lateral) regions for analysis. The algorithm assessed brightness, speckle statistics, and location to select regions. The viability of these identified regions was determined based on the goodness of fit of the LOC calculation and the image quality achieved.

Results & Conclusion: The algorithm yielded a positive predictive value of 96.55%. This indicates reliable identification of viable regions on which to perform the LOC calculation, providing a step toward broad implementation of an automated ALARA tool that could ensure high quality images are being acquired and patient safety is prioritized throughout the scan.

Feasibility of photoacoustic-based intraoperative necrotic region visualization for image-guided catheter RF ablation

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Radiofrequency (RF) catheter ablation is an effective therapy for a wide-range cardiac arrhythmia. However, the current RF systems lack direct, intra-operative, real-time feedback on ablation lesion formation, making assessment difficult. Cardiac magnetic resonance (CMR) can visualize ablation lesions, but its intra-operative usage is still in its infancy. A portable, intra-operative imaging system to visualize the growth of the ablation necrotic region can provide real-time feedback to the operator in the electrophysiology laboratory, and thus is expected to reduce arrhythmia recurrence and procedural complications by avoiding incomplete and excessive ablation, respectively. Photoacoustic (PA) imaging is an emerging biomedical imaging modality based on laser-generated ultrasound. Previous research showed that the PA spectrum of the non-ablated tissue has a prominent hump near 760nm leaning towards the hemoglobin spectrum and is absent in that of the ablated tissue. Based on these findings, we propose a PA image-guided ablation system with a side-firing linear array transducer that enables intraoperative necrotic region visualization. The spectroscopic decomposition process was applied to identify lesions based on spectrum differences. To evaluate our approach, we applied PA imaging to a swine liver before and after RF ablation, using wavelengths of 700nm to 850nm. Direct comparison between the acquired image and gross pathology demonstrates the system can identify the necrotic region. Further, we visualize the continuous colormap presenting the percentage of the ablation extent based on the contribution from the ablated spectra intensity with respect to the total intensity combining with non-ablated spectra, quantifying the ablation extent of the lesion. The measured ablated region thresholding at 60% was 6.2 mm width, matching with the actual lesion width of 5.9 mm. This PA image-guided ablation system has the potential to be incorporated into routine clinical practice by utilizing the standard intra-cardiac echocardiography (ICE) as an ultrasound receiver to guide electrophysiology ablation procedures.

Deep Learning-Based Photoacoustic Visual Servoing

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Tracking needle tips, catheter tips, and surgical tool tips is important for multiple surgical and interventional procedures. Previous work from our group integrated photoacoustic amplitude-based target segmentation with a robot arm to track needle, catheter, and tool tips in multiple imaging environments including fat, muscle, brain, and liver tissue. However, this amplitude-based approach requires the reconstruction of human-interpretable images using delay-and-sum beamforming, which leads to information loss. In addition, performance with beamforming is reduced in the presence of reflection artifacts from bone. As an alternative, we developed a deep learning-based approach to photoacoustic visual servoing, using the Faster R-CNN algorithm with a ResNet-101 backbone to estimate and provide the needle tip position to the robot controller directly from the raw channel data. Our visual servo system consisted of a Verasonics ultrasound scanner interfaced with a Verasonics P4-2v probe, an Opotek Phocus Mobile laser, a 0.6 mm optical fiber inserted into a hollow core needle, and a Sawyer robot. We evaluated our deep learning-based approach with a plastisol phantom and *ex vivo* chicken breast and compared the results to our previous amplitude-based approach. The deep learning approach achieved similar probe centering errors (0.19±0.16 mm and 0.18±0.17 mm in phantom and *ex vivo* tissue, respectively) compared to the amplitude-based approach (0.11±0.12 mm and 0.16±0.14 mm in phantom and *ex vivo* tissue, respectively). In addition, the deep learning approach outperformed the amplitude-based approach with needle tracking error improvements of 67.7% and 55.3% in phantom and *ex vivo* tissue, respectively. These results demonstrate the promise of a photoacoustic visual servo system that bypasses traditional image formation and segmentation steps, instead supplying the robot controller with inputs based on the raw photoacoustic channel data.

The Quantitative Imaging Biomarker Alliance: Medical Imaging Meets Metrology

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Many attendees of this symposium have been involved in the development, implementation, and testing of methods for “tissue characterization”, “parametric imaging”, and “quantitative ultrasound”. Some of this work dates back to the mid-1970’s and before. Our contributions to the Quantitative Imaging Biomarker Alliance (QIBA) are intended to enhance the repeatability and reproducibility of those methods as they near, or have been, commercially implemented on clinical imaging systems. The QIBA approach to this is to apply the principles of metrology (measurement science) to medical imaging. With this, we recognize a hierarchy in the value of information from medical imaging. For example, the observations of an expert observer are more valuable than those of a casual observer, but both are subjective. We build on an objective, quantifiable observation (a measurement) and require specific characteristics of that measurement, such as linearity of the estimates on a ratio scale and known value of the measurand, so that we can estimate the bias and the factors affecting repeatability and reproducibility. These characteristics of the observation allow an estimate of the (eg, 95%) confidence interval on the parameter estimate for different measurement conditions (cross sectional studies, longitudinal studies, etc.). All these considerations go into the selection of quantitative imaging biomarkers pursued by the QIBA organization with the goal of converting these imaging observations to medical assays and will be described in this presentation.

Frequency dependence of the ultrasonic power reflected from cancellous bone

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Background: There is interest in developing ultrasonic techniques that can be used to detect changes in bone caused by osteoporosis and other diseases. Many laboratory studies are performed *in vitro* on specimens of cancellous bone in a water tank. The ultrasonic power reflected from the water specimen interface usually is assumed to be frequency independent. However, this assumption may not be valid due to the porous structure of cancellous bone. The goal of this study was to investigate the frequency dependence of the power reflected from the surface of specimens of cancellous bone in water.

Methods: Pulse-echo measurements were performed on 15 cube-shaped specimens of human cancellous bone in a water tank using four single element, broadband transducers with center frequencies of 3.5, 5.0, 7.5 and 10 MHz. The transducers were mechanically scanned to acquire signals and spectra from multiple locations on each specimen. All six sides of each specimen were scanned. Spectral analysis was performed over a frequency range of 1.5 - 10 MHz to measure the power reflected from the surface of the specimens. The reflected power was corrected for the frequency response of the measurement system by using a polished steel plate as a reference reflector.

Results: The ultrasonic power reflected from cancellous bone exhibited a moderate (< 6 dB) dependence on frequency in which the power increased or stayed approximately the same (depending on specimen porosity) up to 5 MHz, after which the reflected power decreased with frequency.

Conclusions: For frequencies less than 5 MHz, the reflected power is approximately frequency independent for specimens with low to moderate porosities. However, for higher frequencies, and/ or specimens with greater porosities, it may not be valid to assume that the reflected power is frequency independent.

Feasibility of monitoring liver metastases from breast cancer in a mouse model using single transducer-harmonic motion imaging *in vivo*

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Background: Breast cancer is the most frequently diagnosed cancer and 50% of all breast cancer patients develop metastatic disease. Out of all metastatic breast cancer patients, liver metastases develop in approximately 50% of them. If left untreated, liver metastases are associated with poor survival ranging from 4 to 8 months. Early diagnosis or therapy monitoring could help to tailor treatment for individual patients. Change in liver metastases can be monitored via measuring the mechanical properties of the liver. To interrogate the mechanical properties at the “on-axis” to acoustic radiation force, single transducer harmonic motion imaging (ST-HMI) transmits tracking pulses in-between the discrete excitation pulses. The objective of this study is to test the feasibility of monitoring liver metastases from breast cancer in a mouse model using ST-HMI-induced displacement at multiple frequencies *in vivo*.

Methods: The orthotropic, 4T1 breast cancer mouse model (N=6) was generated by injecting 1 x 105 4T1 breast cancer cells in the 4th inguinal mammary fat pad. ST-HMI of both primary cancer and liver was performed at a 7, 10, 13, 20, 26, and 32 days post-injection of tumor cells using Verasonics research systemVantage 256, Verasonics Inc., Kirkland, WA, USA) with L22-14vXLF (Vermon, Tours, France). ST-HMI was implemented with 13 discrete excitation pulses per period after sampling a continuous excitation pulse composed of the sum of sinusoids with 100:100:1000 Hz to interleave tracking pulses with a PRF of 15 kHz. The center frequency of the excitation and tracking pulse was 15.63 and 20.8 MHz respectively. The displacements with respect to the reference frame were estimated using 1-D normalized cross-correlation with a kernel length of 0.77 mm. For each pixel, estimated displacements were filtered out using the 2nd order Butterworth filter followed by the generation of a peak-to-peak displacement (P2PD) image at 100:100:1000 Hz obtained by averaging P2PD values over 5 cycles. Median P2PD values over the region of interest in the primary tumor and liver were computed.

Results and Discussion: In primary tumors, P2PDs were decreased over time which indicates stiffening, and P2PD across time points were statistically different for 100-500 Hz ($p < 0.05$, Kruskal-Wallis). P2PD at 100-500 Hz detected changes in tumor stiffness as early as between 7 versus 10 days. In the liver, P2PD was also decreased over time but the rate was slower than primary tumor which was expected. The Kruskal- Wallis test indicates that the P2PD was different across time-points for 100-200 and 400-700 Hz and P2PD at 400 Hz detected changes in tumor stiffness as early as between 7 versus 10 days. A good correlation was found between the change in P2PD in the primary tumor versus the liver metastases with the highest R2 of 0.72 observed at 100 Hz.

Conclusion: This initial study demonstrates the feasibility of using ST-HMI-derived displacements at multiple frequencies to monitor the progression of both primary tumors and metastases in the liver. Future studies will compare P2PD in the liver between the control group versus the tumor group with histopathological validation.

Comparison of varying acoustic exposure demands between fetal structures

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Introduction: The coherence between neighboring ultrasound array elements, or lag-one coherence (LOC), provides a local measure of clutter. Previous results suggest the trend in LOC observed while varying acoustic output can be used to recommend an acoustic exposure level (mechanical index, MI) that maintains high image quality while achieving the ALARA (As Low As Reasonably Achievable) principle. In this study, the mechanisms that drive the recommendation of different MI values are explored on data collected in multiple fetal organ structures.

Methods: A real-time adaptive transmit intensity adjustment sequence was implemented on a Verasonics Vantage ultrasound system with a GE C1-6D probe. Intensities ranging from 0.1-1.2 MI were swept across a 5-line x 1.5-cm region of interest (ROI) that was selected based on image brightness and SNR. The first MI achieving 98% of the LOC asymptote was recommended for imaging. Acquisitions separately targeting the fetal abdomen, fetal heart, and placenta were performed on 10 pregnant women. The recommended MI and achieved LOC were independently calculated for each structure.

Results: Adjusting intensity based on the data within the ROI resulted in target-specific recommendations for MI. Recommended MIs in fetal abdomen imaging varied between acquisitions and volunteers, ranging from 0.4 to 0.6. In the heart, the average recommended MI was 0.04 higher than the MI used in the abdomen ($p<0.005$), while the MI recommended in the placenta was on average 0.09 below the MI for the abdomen region ($p<0.001$). The acoustic window, the intervening fluid and tissue in the acoustic path, and the underlying uniformity and echogenicity of the target tissue are different for each organ, giving rise to the distinct MI recommendations. Accounting for target-dependent effects is important for achieving predictable and stable results in future adaptive intensity adjustment imaging implementations.

Two Novel Techniques to Estimate the Contribution of Each Scatterer Size in Quantitative Ultrasound

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Background, Motivation and Objective: Effective scatterer diameter can be attained through parametrizing backscatter coefficient using form factor models. However, reporting a single scatterer size cannot accurately characterize a tissue particularly when it contains a broad range of scatterer sizes. Here we present two methods to estimate the scatterer size distribution instead of a single effective size. As a proof of concept, we test the method on theoretical values of the backscatter coefficient obtained from four different distributions of scatterer sizes using Faran theory.

Statement of Contribution/Methods: The scatterer size distribution is estimated using two novel techniques. In the first technique, we cast the estimation of the scatterer size distribution as an optimization problem, and efficiently solve it using a linear system of equations. Starting with a bank of predefined form factors for different scatterer sizes, the resulting form factor for the entire size distribution is a linear combination of the form factors within the bank. Thus, the goal is to estimate the contribution of different form factors and, therefore, the contribution of scatterers of different sizes. In the second method, we use the solution of this system of equations to constrain the optimization function. This is achieved by using the results of the first method to surpass the fluctuations and negative probability observed in the results of the first method. Both methods are tested on mathematically computed backscatter coefficients from Faran theory, from which form factors are derived by dividing by $f4$ and renormalizing.

Results/Discussion: The results show that both methods can estimate different unimodal, uniform, and bimodal scatterer size distributions very accurately, and that the second method outperforms the first one.

Quantification of Skeletal Muscle Fiber Orientation in 3D Ultrasound B-modes Using a Fourier Domain Approach

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Introduction: Complex shear wave propagation has recently been observed in *in vivo* skeletal muscle using ultrasound shear wave elasticity imaging with a 3D rotating setup. Characterization of tissue mechanical properties from measured shear wave speeds requires an accurate determination of muscle fiber orientation (MFO), both in rotation and tilt. Here, we present a Fourier-domain-based algorithm that automatically calculates MFO for 3D B-modes acquired with a rotating setup and with a rectilinear matrix array transducer.

Methods: 3D B-modes of the *vastus lateralis* muscle were acquired *in vivo* using a Verasonics scanner with either an L74 transducer rotated in 5-degree increments or a 1024-element matrix transducer. For each 2D image in the rotating acquisition, a Fourier transform was calculated, converted to polar grid, and summed over a band of radial frequencies. The fiber rotation was the rotational slice with the narrowest peak in the sum, and the fiber tilt angle was perpendicular to the angle that maximized the sum for that rotation. For each 3D rectilinear B-mode, a 3D Fourier transform was calculated, converted to spherical grid, and summed over radial frequencies. The average MFO (ϕ,ϑ) was the direction most perpendicular to the sum projected onto a sphere and was determined with numerical optimization.

Results: The calculated MFOs were compared to fiber orientations measured manually in ParaView software. In a rotating acquisition, the algorithm estimated 13.2° rotation and 10.9° tilt compared to manual values of 13.6±6.4° rotation and 12.1±1.6° tilt. Over 18 such acquisitions, the average error in rotation between the algorithm and a shear wave speed ellipse fit was 4.2°. In a 3D matrix-array B-mode, the algorithm estimated 13.4° rotation and 9.4° tilt compared to manual values of 16.6±7.4° rotation and 9.6±1.5° tilt. Simulated data with known fiber orientations will be used to further validate our methods.

3D SWEI in *in vivo* muscle: what can it tell us?

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Existing methods of shear wave elasticity imaging (SWEI) typically assume an isotropic material; however, a more complex model is required to model skeletal muscle. Our group has previously demonstrated in simulation and *in vivo* skeletal muscle the use of 3D SWEI data to characterize muscle as an incompressible transversely isotropic material. A 3D SWEI approach to skeletal muscle characterization has several advantages, including the ability to automatically align with and account for the direction of the muscle fibers and the ability to observe and measure the multiple wave modes that are generated in transversely isotropic materials. Herein, we extend our 3D SWEI algorithms and explore the effects of muscle contraction. Using a Verasonics scanner and L74 transducer pushing at 4 MHz, 36 acquisitions were taken in the *vastus lateralis* muscle *in vivo* by rotating the transducer around its central axis in 5° increments. From the synthesized 3D SWEI volume, shear wave speeds (SWS) were estimated at all rotation angles. These speeds were fit to an ellipse, with major and minor axes indicating the SWS along and across the fibers. These measurements were repeated under increasing levels of isometric contraction. SWS along the muscle fibers increased approximately linearly with increasing load, while negligible differences were observed in SWS across the fibers with increasing load. We are developing protocols and reconstruction approaches that enable higher order material characterization, including estimating both the shear and tensile anisotropy, as well as approaches for evaluating the viscoelastic properties of skeletal muscle.

High Frequency Ultrasound for Periodontal Soft- and Hard-Tissue Scanning

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Background/Objective Radiological imaging based on x-ray has been and is the dominant modality in dentistry. Radiographs and cone-beam CT (CBCT) are accepted state of the art techniques for visualizing tissue structurally. Large contrast and unhindered penetration are obtained when displaying hard-tissue, but ionizing radiation and image artifacts are of concern. Ultrasound may be a complementary cross-sectional imaging modality, as it yields high soft-tissue contrast and is able to image bone widths adjacent to implants without image degradation.

Methods A now commercially available intra-oral high frequency linear array transducer has been developed. At 18 MHz center frequency, axial and lateral (f#3) resolution of 85 and 256 µm, respectively, are feasible. Typical 2D image orientations are sagittal, i.e., extend from the gingiva to the crown and display the surfaces of the visually covered jawbone and tooth root or the abutment/implant of an artificial tooth. Available image modes include harmonic/compounded B-mode, color flow and pulsed wave. Diagnostic soft- and hard-tissue measurements (interdental papilla height, soft tissue height at teeth, mucosal thickness at teeth, soft tissue height at the edentulous ridge, mucosal thickness at the edentulous ridge and crestal bone level) at and adjacent to 40 teeth and 20 tooth gaps were assessed in 20 patients. Three modalities are compared, ultrasound, CBCT (resolution 0.2 to 0.5 mm) and direct (ruler based).

Results/Discussion In comparison to direct measurements, ultrasound outperformed CBCT for every measurement (except for edentulous ridge evaluation where CBCT was not available). In the above diagnostic tissue measurements order, ultrasound to direct differences were -0.076, -0.159, -0.015 and -0.078 mm, whereas CBCT to direct were 0.351, 0.455, -0.213, and 0.412 mm. Ultrasound to direct differences for edentulous ridge evaluation were 0.479 and 0.127 mm. Ultrasound has shown to be a precise diagnostic tool for tissue dimensional assessment with high soft-tissue contrast and no ionizing radiation.

Comparison of two plane wave compounding strategies for 3D-SWEI using a rectangular matrix transducer

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Introduction: Shear wave elasticity imaging (SWEI) uses an acoustic radiation force impulse (ARFI) push to excite micron-level displacements in tissue. Plane wave (PW) imaging provides the high frame rates (~10 kHz) necessary for SWEI tracking. To fully characterize transversely isotropic materials (such as muscle), shear wave monitoring in 3D is necessary. We are developing a 3D-SWE imaging system that uses a rectangular matrix array (16x64 elements). Here, we assess the ability of our matrix probe to monitor shear wave propagation in 3D exploring tradeoffs between coherent compounding methods in simulation studies, as well as evaluating interpolation methods to overcome the lower PRFs associated with the compounding methods.

Methods: Tissue displacements were simulated using finite-element models assuming a 12-kPa linear elastic solid and an 87-microsecond ARFI excitation. The resulting displacements were used to displace a field of random scatterers over a period of 10 microseconds sampled at 10 kHz in Field II, where PW imaging in different angle combinations, (-3°, 0), (3°, 0), (0, 0), (0, -3°), (0, 3°), for each time step was simulated. The two PW compounding strategies compared here are single-push multiple angle (SPMA) requiring a single push and a running window sum, and multiple-push-single angle- per-push (MPSA) realizing full PW compounding. Displacements were calculated using Kasai's algorithm and group shear wave speeds were estimated using a Radon sum algorithm. We also evaluated interpolation methods to address the inherent tradeoff between PRF and compounding through a phantom study evaluating PRFs ranging from 0.5 kHz to 10 kHz, spaced by 0.5 kHz.

Results: The rectangular-aperture probe modeled is robust for shear wave tracking in 3D. SPMA breaks down faster than MPSA at low PRFs. Additionally, at low experimental PRFs, it is feasible to use interpolation to recover a high-frame-rate compounded dataset, which improves group shear wave speed estimation accuracy.

Frequency compounding in spatial coherence-based beamforming

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Introduction: Spatial coherence has found wide use in image quality characterization and beamforming. Our lab has shown that the coherence measured between neighboring elements may be used to (1) estimate the level of clutter, and (2) adaptively filter images in a method known as Lag-one Spatial Coherence Adaptive Normalization (LoSCAN) [1,2]. LoSCAN has been shown to boost image quality in cluttered acoustic environments. Here, we assess additional improvements when coherent frequency compounding is applied to images filtered with LoSCAN.

Methods: In 25 patients recruited at the Duke Fetal Diagnostic Center, channel data were collected for a series of frames at 8 different transmit frequencies spanning a bandwidth from 2-5 MHz, using the Verasonics Vantage system with a C5-2v array. Channel data were time delayed and filtered with center frequency matching the transmit frequency, or double in harmonic cases. LoSCAN was performed on the resulting data, then coherently compounded over frames acquired at different transmit frequencies. Contrast and CNR were calculated using the fetal stomach as a hypoechoic structure and surrounding homogeneous fetal abdomen regions as the reference.

Results: Preliminary results indicate that frequency-compounded LoSCAN offers greater improvements in image quality than frequency-compounded B-mode and single frame LoSCAN. 90% of patients showed at least a 10% improvement in both contrast and CNR with frequency-compounded LoSCAN, compared to 23% in the frequency-compounded B-mode cases and 36% in the single frame LoSCAN cases. Future work will explore using less pulse-echo frames for compounding to improve imaging frame rates, as well as investigate the use of multiple filter banks to supplement the number of frames per pulse-echo event.

[1]: Long, W. et al. Lag-one coherence as a metric for ultrasonic image quality. *IEEE TUFFC*, 2018.

[2]: Long, W. et al. Incoherent clutter suppression using lag-one coherence. *IEEE TUFFC*, 2020.

In vivo evaluation of nonalcoholic steatohepatitis using spectral quantitative ultrasound and envelope statistics parameters in mice

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The gold standard for diagnosing nonalcoholic steatohepatitis (NASH) has been liver biopsy. As such, non-invasive and serially applied methods of diagnosis capable of quantifying fat content and fibrosis severity in the liver are highly desirable. This study's objective was to evaluate the correlation of quantitative ultrasound (QUS) parameters to *in vivo* measurements of liver fat fraction using magnetic resonance imaging (MRI) and dual energy X-ray absorptiometry (DEXA), as well as to fat content, inflammation, and fibrosis quantified from histopathology. Forty mice were used in this study, divided evenly between male and female. Twenty mice were controls using a standard low-fat chow (SC) diet. NASH was induced in the remaining twenty mice using a fructose/glucose/cholesterol-enriched diet. The livers were imaged *in vivo* using a Vevo 3100 scanner and MX550D transducer, with a 25-MHz measured center frequency. The livers were also examined with whole body cryogen-free Bruker Biospec 3-Tesla MRI to estimate liver fat fraction using the two-point Dixon method, as well as with the Lunar Piximus DEXA scanner, the non-invasive gold standard. QUS methods were used to compute the spectral slope (SS), intercept (I0), midband fit (MF), effective scatterer diameter (ESD), effective acoustic concentration, and homodyned K scatterer clustering parameter (α) and structure parameter (κ). Pearson's correlations (R) of QUS parameters to MRI-determined liver fat fraction were calculated. P-values < 0.05 were considered statistically significant. The largest, statistically significant correlation to MRI-determined fat fraction was achieved with α in females (R=0.83), and with MF and I0 parameters in males (R=0.61). Although further correlations are underway with *in vivo* DEXA measurements as well as histopathology measurements of fat and fibrosis, these results demonstrate that QUS methods may be useful as a fast and low-cost imaging tool for screening and estimating liver fat fraction *in* vivo through non-invasive methodologies.

Continuous Wave Doppler Ultrasound to Detect Muscle Fatigue

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Functional electrical stimulation (FES) is commonly used in physical rehabilitation, bypassing the central nervous system to activate motor neurons directly. However, the unnatural muscle recruitment pattern induced by FES causes rapid muscle fatigue, greatly reducing the muscle's ability to generate force. Currently there exists no reliable, real-time indicator for FES-induced muscle fatigue. We believe that signs of muscle fatigue can be inferred from medical ultrasound. Previously we investigated tissue Doppler imaging (TDI) to study muscle physiology associated with muscle potentiation and fatigue. Here we expand on that research using continuous wave (CW) Doppler ultrasound to create a wearable, low power muscle fatigue monitor. We are investigating this system to work with a hybrid FES exoskeleton designed to use the patient's own muscles with FES with the added stability of an exoskeleton. CW ultrasound indicated that the duration of muscle recruitment decreased from 129.0ms to 51.7ms for the same FES as the muscle fatigued. Further, we showed that muscle twitch duration and velocity correlate with twitch force, a marker of fatigue recovery, using TDI and CW. These fatigue and recovery measures can be used to inform the exoskeleton controller to coordinate FES and electric motors for producing gait.

Muscle characterization with Ultrasonic Echo Intensity and Fractal Dimension and their Diagnostic Performance for the detection of Frailty Phenotype

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Although muscle echo intensity (EI) has been proposed as a biomarker for the diagnosis of frailty, so far, no studies have explored it´s diagnostic performance. Fractal dimension (FD) can play an important role for modeling different organs in ultrasound studies, and since muscles have fractal properties, it could help to characterize muscle further with imaging. We assessed muscle EI and FD from muscle ultrasound to determine the relationship between the two variables, and their diagnostic capability to identify frailty phenotype. A retrospective interpretation of ultrasound scans from a previous cohort was performed. The sample included healthy participants <60 years old, and participants ≥60 divided into robust, pre-frail, and frail groups according to Fried frailty criteria. A region of interest of the *rectus femoris* from the ultrasound scan was segmented, and histogram function was applied to obtain EI. Images were also processed using two-dimensional box-counting techniques to calculate FD. Statistical analyses were performed with diagnostic performance tests. A hundred and two participants (mean age 63±16, 57 men) were evaluated. The main results showed that muscle FD correlated with EI ($r = 0.38$, $P < 0.01$) and showed different patterns according to frailty phenotype. The diagnostic performance for EI to categorize frailty as present or absent was good (AUC of 0.69 95%CI 0.59-0.78, $P = 0.001$). However, the diagnostic performance for the combination of both EI and FD resulted in no improvement of the diagnostic performance (AUC of 0.58 A.U., 95%CI: 0.46-0.68, $P = 0.18$). In conclusion, we determined that EI was useful to identify individuals at risk of frailty, and while FD did not improve the detection of frailty, it was able to characterize the individuals further by reflecting changes in the muscle that likely reflects the known frailty-related muscle dysfunction secondary to degeneration of the muscle architecture. This allowed us to dichotomize our sample in the most appropriate way for the identification of frailty and improve EI as a possible diagnostic tool for frailty phenotype.

Ultrasonic attenuation as a biomarker for liver steatosis: an AIUM/QIBA perspective

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The high prevalence of Non-alcoholic fatty liver disease (NAFLD), about 25% of the global population, has necessitated quantitative imaging tools [1]. NAFLD is characterized by steatosis, excessive deposition of fat in the liver, commonly referred to as a fatty liver disease. Liver biopsy is the clinical standard for diagnosing NAFLD and grading steatosis. However, the biopsy is limited by cost, high sampling variability, and procedure associated morbidity restricting repetitive use. Although ultrasound is the first line of imaging modality for diagnosing NAFLD, the current practice is based on sonographic hepatorenal index leveraging the increased liver brightness due to fat deposition in comparison to the kidney. The practice suffers from user subjectivity, non-quantitative, and low sensitivity in the detection of mild steatosis, 60.9%-65% [2, 3]. Ultrasonic attenuation is the loss of ultrasound energy as the acoustic wave propagates in soft tissue. Estimation of local ultrasonic attenuation provides information regarding the underlying nature of the soft tissue. Fatty tissue is known to be more attenuative than normal liver tissue; thus, a local attenuation estimate can act as a surrogate marker for liver steatosis. With the maturity of technology, the stage for attenuation to become clinically adopted has been set. Ultrasound vendors are following suit and most of the ultrasound vendors have already introduced attenuation estimation techniques in their flagship models. However, before the wide clinical adoption of attenuation as a biomarker for fatty liver disease, there is a need to standardize attenuation measurement, understand sources of bias and variance, improve data quality, and reach a consensus on reporting attenuation values. The AIUM/QIBA Pulse-Echo Quantitative Ultrasound (PEQUS) attenuation workgroup is seeking to provide guidance on key attenuation parameters such as transmit center frequency, region of interest, depth, and frame rate. In addition, good practices guidance for acquiring attenuation estimates, displaying results, and calibrating systems will be provided. Finally, the attenuation variability within a system, between systems, and between operators will be documented using customized, well-characterized phantoms.

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Ultrasonic parametric imaging of brain tissue using the backscatter difference technique

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Background & Objective: Transcranial ultrasonic backscatter can, in principle, be used to analyze brain tissue properties non-invasively. The main challenge involves errors associated with ultrasonic attenuation and distortion of the ultrasonic wave front by the skull. A newly developed backscatter difference technique may be relatively insensitive to these errors. The goal of this study was to generate parametric images of brain tissue based on three backscatter difference parameters called the normalized mean, slope, and intercept of the backscatter difference (nMBD, nSBD and nIBD respectively). Each parameter measures an aspect of a power spectrum derived from the spectral difference between two portions of the same backscatter signal.

Methods: Tissue specimens used in the study were 1 cm thick slices of preserved sheep brain prepared from the coronal, sagittal and transverse anatomic planes. Pulse-echo measurements were performed in vitro using broadband, single-element transducers with center frequencies of 3.5, 5.0, 7.5 and 10 MHz. The transducers were mechanically scanned with a step size equal to one-half of a beam diameter to acquire data from all locations on each slice. Values of nMBD, nSBD and nIBD measured at each location were used to produce parametric images of the brain specimens.

Results: Structures visible in the parametric images were consistent with anatomic features of the brain. Depending on the tissue slice and transducer frequency, measured mean values ranged between -0.134 and 2.04 dB·µs-1 for nMBD, -0.245 and 1.523 dB·µs-1·MHz-1 for nSBD, and - 0.425 and 2.152 dB·µs-1 for nIBD.
Conclusions: These results lay the groundwork for transcranial ultrasonic backscatter measurements of the brain by providing baseline measurements of nMBD, nSBD and nIBD for brain tissue. Future work will compare these results to measurements made through skull bone.

Quantitative Viscoelastic Response (QVisR) ultrasound in mechanically heterogeneous inclusions

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Background: Point-wise, on-axis estimation of viscoelasticity would allow a finer resolution and relaxed region homogeneity assumptions when compared with shear wave based elastography methods. QVisR was previously validated *in silico* with mechanically homogeneous, isotropic, linearly viscoelastic materials. This work extends QVisR to mechanically heterogeneous materials, *in silico*.

Methods: We simulated viscoelastic materials with spherical inclusions subject to an applied double-push VisR sequence with ultrasonic tracking using a combination of Field II and Ansys LS-DYNA. A Siemens VF73 transducer was modeled to push and track at focal depths from 15-35mm in steps of 5mm. The double-push VisR sequence was applied to 16 material combinations where the background shear elastic and viscous moduli were fixed (8.7kPa and 0.78Pa.s) while the inclusion shear elastic and viscous moduli varied (5.18-12.22 kPa, 0.003-1.30 Pa.s). The inclusion was shifted laterally in 4 increments (0, 2.5, 4, 7mm) to interrogate the effects of the lateral inclusion boundary on the applied force distribution. The resulting FEM nodal displacements were translated to 5 randomly initialized scatterer fields and then ultrasonically tracked. White Gaussian electronic noise (20-50dB SNR) was added to the simulated RF lines before tracking with normalized cross correlation. In total, 11.2 million tracked displacement time series were simulated, added to the previous QVisR homogeneous material dataset, and then split into train/validation/test sets for machine learning model training and evaluation.

Results and Conclusion: The test set RMSEs for shear elastic and viscous moduli estimation were 0.265kPa and 0.084Pa.s, respectively. Future work will target model generalization to phantoms and *in vivo* application.

Analytic Global Regularized Backscatter Quantitative Ultrasound

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Background, Motivation and Objective: Previous studies have demonstrated that regularized cost function improves the estimation of quantitative ultrasound (QUS) parameters. Moreover, our group has recently proposed optimizing a regularized cost function using dynamic programming (DP) based method to accurately estimate effective attenuation coefficient and the backscatter coefficient. However, as DP is a discrete optimization method and requires pre-defined search ranges, it encounters some major issues particularly in clinical applications. To tackle these difficulties, we were motivated to propose a new strategy.

Statement of Contribution/Methods: We analytically solved a regularized cost function to estimate the effective attenuation coefficient and the backscatter coefficient. We referred to the new method as AnaLytical Global rEgularized BackscatteR quAntitative ultrasound (ALGEBRA) and performed the estimation using two versions of that. The first technique, 1D-ALGEBRA, minimizes the same cost function as the DP method and provides an optimal solution using regularized cost function applied in the axial direction while 2D-ALGEBRA exploits a global regularization.

Results/Discussion: We showed that our proposed techniques can estimate the effective attenuation coefficient and the backscatter coefficient very accurately and precisely, and that the second version outperforms the first one, additionally, it is up to 600 times faster than DP in phantom experiments.

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Ultrasound multiple scattering as a source of contrast to quantify pulmonary edema and localize lung nodules

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CT imaging is a common and reliable technique for lung diagnosis. However due to portability, rapid imaging, cost, and absence of irradiation ultrasound is becoming an option for thoracic imaging, especially for monitoring chronic diseases such as pulmonary edema, or during surgery, where real-time imaging is needed. Because of multiple scattering of ultrasound in the parenchyma, conventional ultrasound imaging leads to artifacts that do not reflect the true anatomy of the lung. Although these artifacts are related to lung damage, they are qualitative and not specific. We can capitalize on multiple scattering to quantify changes in lung structure. In a highly scattering medium such as lung, the wave undergoes a diffusive regime. Because of the presence of fluid buildup, edematous lungs are expected to generate less scattering than healthy lungs. This can be quantified by measuring the scattering mean free path (SMFP). Similarly, the presence of nodules inside the lung can be detected since lung nodules do not exhibit air-filled alveoli and are not expected to generate multiple scattering. In this study, using a linear transducer array and Verasonics Vantage ultrasound scanner, we compared edematous and healthy rat lungs in-vivo and ex-vivo. We demonstrate that SMFP can distinguish between 6 edematous lungs and 6 control lungs. Furthermore, artificial nodules were injected in pig and dog lungs ex-vivo. We demonstrate that is it possible to use multiple scattering as a source of contrast to detect and localize nodules. We successfully managed to detect nodules in 7 animals (90% detection rate, 100% in the last 4 lungs). This presentation is an overview to show the feasibility of quantitative ultrasound in the parenchyma.

Biomarker Science – A framework for the AIUM/QIBA Pulse-Echo Quantitative Ultrasound Biomarker Committee

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Quantitative imaging (QI) is at the center of precision medicine, providing clinicians with objective information about tissue structure and function that can potentially be used in personalized diagnosis, staging, prognosis, and prediction of treatment outcome. This new paradigm, initially explored in oncology, is now being extended to other fields in medicine. Key elements in QI are quantitative imaging biomarkers (QIBs), defined as quantitative features extracted from medical images that can be used as surrogates of the normal or pathological state of tissue. This talk will cover the key principles of biomarker science and will provide a framework through which biomarkers can be understood. This will be followed by a discussion on the concepts of imaging biomarkers, quantitative imaging biomarkers, biomarker performance characteristics and how an understanding of these is crucial for clinical practice and the efficient development of therapeutics. The talk will direct this framework to the efforts of the AIUM/QIBA Pulse-Echo Quantitative Ultrasound (PEQUS) Biomarker Committee, which is working to standardize the implementations of PEQUS-based QIBs that have been or are soon to be commercially and clinically deployed for the non-invasive assessment of fat infiltration in the liver. These QIBs include the acoustic attenuation, backscatter, and sound speed. This talk will be followed by presentations from the four working groups that constitute PEQUS, each of which will present a historical perspective and current challenges regarding the clinical translation of each of the biomarkers, as well as on the design of tissue-mimicking phantoms for biomarker standardization and validation.

We are grateful to Kelly Phillips and Therese Cooper for their efforts in coordinating the logistics of the PEQUS Biomarker Committee.

Characterization of the viscoelastic properties of polyvinyl alcohol (PVA) phantoms for ultrasound elastography

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Background and objective: Polyvinyl alcohol (PVA) cryogels are used extensively as tissue-mimicking phantoms in ultrasound elastography. The ability to modify the viscoelastic properties of these cryogel phantoms is necessary to evaluate the performance of elastography techniques. Addition of glycerol has been shown to modify the viscosity of fluids and speed of sound of hydrogels. The objective of this study was to assess the acoustic and viscoelastic properties of PVA phantoms without and with glycerol at varying concentrations.

Methods: Cryogel phantoms were fabricated with 10% w/v PVA in water and either 0%, 10% or 20% v/v of glycerol. The phantoms underwent either one, two, or three 24-hour freeze-thaw cycles. Silicon carbide (2% w/v) was used to enhance acoustic scattering. Three samples were tested for each combination of phantom composition and freeze-thaw cycle. The speed of sound and acoustic attenuation coefficient were determined using a broadband through-transmission system (5–18 MHz bandwidth). The storage and loss moduli were measured using a rheometer (MCR 302, Anton Paar, Austria).

Results: The speed of sound and acoustic attenuation coefficient of all phantoms was between 1497-1500 m/s and 0.5-0.7 dB/cm/MHz, respectively. These results are consistent with the values reported for soft tissues. Addition of 10% glycerol to PVA phantoms decreased both storage and loss moduli, whereas the addition of 20% glycerol increased both storage and loss moduli.

Conclusion: The acoustic and viscoelastic properties of PVA cryogel phantoms can be tuned to the range reported for healthy and diseased tissues. Varying concentrations of glycerol can be used to attain the viscoelasticity of the tissue of interest, which is expected to be useful for performance characterization of ultrasound elastography.

Acoustic reciprocity applied to spatial coherence imaging

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Background and Aims: Due to higher rates of obesity in recent years, transthoracic echocardiography increasingly suffers from poor visualization. Previously, Harmonic Spatial Coherence Imaging (HSCI) has been shown to improve visualization in difficult to image patients. HSCI is an alternate image formation method that uses spatial coherence across received channel signals. However, most clinical scanners are not capable of outputting channel data. We propose applying the principle of acoustic reciprocity to enable use of HSCI on existing clinical scanners while reducing HSCI computation times.

Methods: Applied to synthetic aperture beamforming, acoustic reciprocity states that spatial coherence across receive channels is equivalent to spatial coherence across transmit channels. For focused-transmit synthetic aperture, we can similarly calculate the spatial coherence across signals from focused transmits that have been receive beamformed along the same image line. This method allows us to take advantage of scanners' existing pulse sequencing and parallel receive beamforming capabilities. We validated this method on Field II simulated lesions and a tissue-mimicking phantom.

Results: The generalized contrast-to-noise ratio (gCNR) is 0.65 for the B-mode image of the lesion phantom. For spatial coherence imaging, gCNR values are 0.90 and 0.77 for the control case and the acoustic reciprocity case, respectively. Simulated lesions yielded similar results to the phantom experiment. In terms of spatial coherence computation time, calculations for a single frame took 46.4s for HSCI and 10.6s for acoustic reciprocity HSCI (n=10) using unoptimized MATLAB code. Acoustic reciprocity is qualitatively similar to subaperture approaches in HSCI.

Conclusion: Acoustic reciprocity spatial coherence imaging trades off noise reduction with computational speed. With optimization, acoustic reciprocity HSCI is a feasible method for translation of HSCI to clinical scanners.

An optimization of volumetric transrectal ultrasound imaging using radial synthetic aperture focusing: a closed-form analytic solution

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Volumetric transrectal ultrasound (TRUS) has been an essential modality in clinics for accurate identification and biopsy guidance of prostate tumor, in which multiple radial planes of target volume are sequentially acquired by mechanical angular scanning. Here, we present a quantitative design guideline of radial synthetic aperture focusing framework for high-definite and high-sensitive volumetric transrectal ultrasound imaging (TRUS-rSAF). A closed-form analytic solution provides a theoretical foundation defining critical imaging parameters: virtual source position $felv$, aperture size *h*, and transducer radius *r*. The individual characterization of the parameters gives quantitative perspectives on how to optimize the TRUS imaging system. As a result, having shallower $felv$, larger *h* and *r* provide better spatial resolution as these contribute to larger synthetic window formed with wide divergence of transmitted beam. In addition, SNR improvement of TRUS-rSAF was evaluated in our simulation platform, where the coherent frame compounding within the synthetic window increases the sensitivity of the image. Consequently, the integrated optimization was conducted to obtain the ideal spatial resolution (i.e., $felv$ /*h*/*r* = 5mm/7mm/15mm) and was comparatively evaluated in clinical scenario (TRUS-REF, 25mm/5mm/10mm). B-mode image evaluation demonstrated that the optimized TRUS-rSAF showed superior spatial resolution at all depth compared to TRUS-REF. However, the spatial resolution-oriented optimization yielded low SNR at deep imaging depths due to the diverging acoustic profile to secure wider synthetic window and grating lobes caused by coarse radial sampling. To secure the SNR comparable to what offered in TRUS-REF imaging, we adjusted the scanline density to control the grating lobe positions and increase the number of synthesize for suppressing the noise level. In addition, corresponding temporal resolution was also analyzed. In summary, the comprehensive analysis offered a framework to balance the spatial resolution and signal sensitivity of the TRUS-rSAF imaging, with consideration on clinical expectation given in conventional volumetric TRUS imaging.

Development of phantoms for study of variation in measurements of quantitative ultrasound parameters: A QIBA/PEQUS perspective

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Non-alcoholic fatty liver disease (NAFLD) is a significant condition worldwide. The current standard of diagnosing NAFLD is liver biopsy. Quantitative ultrasound has been proposed as a less invasive method for measuring liver fat. Studies indicate that progression of disease may involve changes in speed of sound, attenuation coefficient, and backscatter coefficient of liver tissue. Several ultrasound scanner manufacturers have developed or are in the process of developing methods for in-vivo estimations of one or more of these parameters, with the goal of measuring liver fat. AIUM/QIBA created a Pulse-Echo Quantitative Ultrasound (PEQUS) biomarker committee to study these measurement techniques, determine correlations and cofounders, and minimize variance. The PEQUS Phantom Workgroup was tasked with designing and procuring phantoms for this purpose. Phantom specifications were chosen to mimic the range of acoustic properties observed across the spectrum of fatty liver disease severity. These phantoms will be constructed using standard tissue-mimicking gels with embedded microbeads. The phantoms will be used in a multi-institution, round-robin study of measurement variability utilizing a variety of data acquisition platforms and analysis algorithms. These include methods that are commercially available on scanners, methods that require offline analysis of RF data acquired from commercial or research scanners, and lab-based methods using pulse-echo and through transmission analysis employing single element transducers. Approximately 40 international sites have expressed interest in participating. Two sets of phantoms with identical specifications will be produced, one set from CIRS (Norfolk, VA) and one from Sun Nuclear (Middleton, WI). These phantoms will be shipped between sites, with a total time for acquiring data from all laboratories of about 8 months. The sets of phantoms will be compared against each other at several sites and compared for changes in acoustic properties before and after the round robin study.

Is piezoelectricity in bone due to collagen?

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Background: Fukada and Yasuda reported that electrical potentials were generated inside bones when low-frequency mechanical stress was applied. One possible mechanism is the contribution of collagen in bone.1 The purpose of this study is to examine the piezoelectricity of type 1 collagen in the MHz range, to check the contribution of collagen on the bone piezoelectricity.

Methods: Using a disk shape collagen sheet (diameter; 11 mm, thickness; 40 μm, uniaxial collagen fibers align in the plane, Atree Inc.), we fabricated a collagen transducer as an ultrasound receiver. Burst ultrasonic waves with 10 sinusoidal cycles of 7.4 kPa peak-peak at 1 MHz were irradiated to the transducer. The received signals at the collagen transducer were amplified 40 dB by a preamplifier and observed using an oscilloscope. The transducer was first set on the acoustic axis (0 degree) of the transmitter and gradually moved to the off-axis positions in the plane parallel to the fiber orientation direction.

Results and Conclusion: The collagen transducer showed the highest electrical output at around −40 and 45 degrees, and the minimum at around 0 degree, thus demonstrating the piezoelectric anisotropy of collagen. The amplitude of electrical potential obtained by the collagen transducer was almost the same to that of bone transducer. The anisotropic character was similar to bone 2 and showed that bone piezoelectricity was likely due to collagen.

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Estimation of Homodyned K Distribution Parameters Using A Statistically Regularized Convolutional Neural Network

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The homodyned k (HK) distribution is the most comprehensive distribution that can model different ultrasound echo amplitude measured distributions including fully developed, underdeveloped and coherent speckle. The estimation of the parameters of this distribution (α, k) has attracted great attention for tissue characterization since these parameters are highly correlated with physical properties of the tissue. The parameter α is mostly sensitive to the number density of scatterers within the resolution cell, whereas k characterizes the ratio of the coherent to diffuse components of the echo amplitudes. In this paper, we propose a convolutional neural network (CNN) approach for simultaneously estimating α and classifying k. To that end, we generated a large dataset of independent samples of the HK distribution consisting of 15,000 patches having 32,768 independent samples. We then trained a CNN to estimate $\log(\alpha)$ and classify the k parameter into noncoherent ($k=0$) and highly coherent (k=1). To constrain the network, we used statistical prior knowledge (SNR, skewness, X, U and kurtosis) as multi-task learning to avoid over-fitting of the network. We presented the results for 18 frames of three experimental phantoms having high, medium, and low scatterer densities (therefore, high, medium, and low values for α are expected, respectively). There is no coherent scattering hence the value of k should be low for all frames of the three phantoms. The mean value of α were 4.85, 1.95 and 0.55 for high, medium, and low-density phantoms, respectively. The mean probability of coherency of the phantoms were 5e-10, 1e-5 and 0.057 for high, medium, and low-density phantoms, respectively. In future work, we plan to apply our method on highly coherent phantoms.

Speed of Sound Measurement to Quantify Hepatic Steatosis: An AIUM/QIBA perspective

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Nonalcoholic fatty liver disease (NAFLD), characterized by fat deposition in the liver, is a leading cause of fibrosis, cirrhosis, end-stage liver disease, and subsequent liver transplantation in the United States and worldwide. There is an urgent need for safe, widely available, low-cost, accurate, and reproducible quantitative markers of liver fat concentration to robustly diagnose NAFLD, assess disease progression, determine indications for therapy, and assess treatment response. The speed of sound (SoS) in liver, measured by medical ultrasound, is a quantitative parameter correlated with hepatic fat fraction. The AIUM/QIBA Pulse-Echo Quantitative Ultrasound (PEQUS) group presents a literature review of sonographic SoS estimation techniques to identify those with near-term potential of noninvasively measuring hepatic SoS in vivo as a biomarker of steatosis. Of the ten estimation techniques reviewed, the three most promising were focusing, compounding, and spatial coherence. Focusing methods estimate the SoS by adjusting the beamforming to maximize image quality metrics, such as lateral resolution. Compounding methods estimate the SoS by applying varying transmit beam directions to measure the resultant local phase changes. Spatial coherence methods estimate the SoS by maximizing the coherence of echoes from a target region. Hepatic SoS varies from 1450 m/s to 1650 m/s depending on the underlying pathology. Normal liver SoS is about 1540 m/s, while steatotic livers have a lower SoS and cirrhotic livers have a higher SoS. Studies using ultrasound SoS have shown high measurement precision, reliability between operators, and accuracy compared with pathology or magnetic resonance proton density fat fraction measurements. Likely confounders for SoS measurement include liver fibrosis, subcutaneous fat effects, and depth dependence of some techniques. While promising, additional studies are needed to standardize the measurement of hepatic SoS, determine the expected variability of the quantitative outputs, confirm correlation with hepatic fat and fibrosis levels, and delineate diagnostic thresholds.

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Improving diagnostic certainty in breast ultrasound with coherence-based beamforming

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Ultrasound imaging is often used for the diagnosis of breast cancer. However, the false positive rate of breast ultrasound can be as high as 93%, often because standard B-mode images display amplitude information which is highly susceptible to the presence of acoustic clutter. Acoustic clutter confounds these images, causing fluid-filled masses to appear solid and to be unnecessarily recommended for biopsy. This work investigates the clinical impact of coherence-based beamforming to remove acoustic clutter and improve distinction between solid and fluid breast masses. Twenty-five patients with twenty-six masses scheduled for biopsy were enrolled in our study after informed consent and approval from the Johns Hopkins IRB. Patients were scanned using an Alpinion ECUBE12R ultrasound scanner with either an L8-17 or L3-8 linear ultrasound transducer. Raw data were processed offline to generate matched B-mode and coherence-based images for each mass of interest. The matched images were presented to five board-certified breast radiologists who were asked to use only the B-mode image to perform two tasks: (1) classify the content of the mass (i.e., solid, fluid, mixed, or uncertain) and (2) provide a clinical diagnosis (i.e., BI-RADS 2, 3, 4 or 5). Following classification with only B-mode, the radiologists were presented with the coherence-based image and asked to perform the same two tasks. With the inclusion of coherence-based images in decision making, the uncertainty of fluid-filled mass contents was reduced from 47% to 15.8%, and the percentage of fluid-filled masses unnecessarily recommended for biopsy was reduced from 43.3% to 13.3%. The mean sensitivity for detection of fluid-filled masses was improved from 57% with B-mode alone to 86% with the addition of coherence-based images. These results are promising for using coherence-based beamforming to improve diagnostic certainty in the breast clinic and to reduce the number of unnecessary biopsies.

High--resolution quantitatively accurate full-wave 3D ultrasound tomography with 64X speed-up

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Introduction: We present tissue characterization with ultrasound tomography (UT). Historically it has not been clinically relevant due to its failure near bone and air and long reconstruction times. 2D algorithms can create 3D volume images from 'slices', as in classical tomography, in 10's of seconds but have artifacts. 3D reconstruction codes require ~32 hours using a 128 cluster of CPUs. We have reduced the time by a factor of 64 – 256 using only two NVIDIA GPUs.

Method: Our 3D algorithm emulates the training of a gauge equivariant fully connected Neural Network and therefore runs optimally on NVIDIA GPUs. The 3D algorithm runs on 2 NVIDIA RTX6000s and yields the image in 8 – 30 minutes depending on subject's or organ's size which we show. We compare our SOS values with the literature for human muscle, tendons, ligament, prostate, cartilage, fat, prostate, skin, ductal and glandular tissue, and ovine liver by segmenting 6 mm dia. Regions of interest (ROI) of interest.

Results: We show quantitative accuracy for the bulk modulus (speed of sound) even in the presence of bone. Upon segmentation, the standard deviations vary from 0.88% to 2.2% and fall within literature bounds except for collateral ligaments. We also compare MR images to validate UT morphology for breast, pig, and knee even in the presence of bone. Published values for similar algorithms require a cluster of 128 computers and ~32 hours: 64X more compute nodes and 64X more time, for a total complexity factor of 4096X.

Conclusion: The time required is clinically relevant and requires only two NVIDIA GPUs; therefore, the UT scanner is ideal for Low Resource Environments. The images are quantitatively accurate with 0.62 mm resolution.

Consecutively versus Simultaneously-tracked Displacement Profiles for Double Profile Intersection (DoPIo) Ultrasound

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Background: Double-Profile Intersection (DoPIo) ultrasound estimates shear elastic moduli on-axis, pointwise, by exploiting differences in acoustic radiation force impulse (ARFI)-induced displacements measured using two different tracking focal configurations. The differences arise from scatterer shearing under the tracking PSF caused, in part, by the relationship between ARFI and tracking beam focal configurations. We evaluate whether DoPIo's performance can be improved by simultaneously beamforming two different tracking beams so identical scatterer realizations are represented in the compared displacement profiles.

Methods: Using the FEM software LS-DYNA, ARFI excitations focused at 25mm were applied onto homogeneous, elastic materials, and displacements were tracked using normalized cross correlation applied to Field-II-generated RF data. To simulate consecutive tracking, transmit and receive apertures were matched at F/1.5 or 3.0 to interrogate different scatterer realizations, each with a density of 1250/mm3 (25/resolution cell for F/# 1.5 at 6.15MHz). The times when the two resulting displacement profiles intersected were inputted into an empirically derived linear model to estimate moduli. To simulate simultaneous tracking, an F/3 transmit and F/1.5 or 3.0 receive was used to interrogate the same scatterer realizations with the density described above. The resulting displacement profiles were used as described for consecutive tracking to estimate shear elastic modulus, and estimated moduli were compared between consecutive and simultaneous tracking.

Results/Conclusion: For materials with true moduli from 3kPa to 35kPa, the median ± MAD errors of elasticity estimates were 0.3±0.7kPa for simultaneous tracking, versus -10.4±0.1 kPa for consecutive tracking. Modulus underestimation in simultaneous tracking arose in materials stiffer than 15kPa, where Bonferroni-corrected ANOVA failed to distinguish elasticities within 8kPa. This range lowered to 4kPa for simultaneous tracking, and simultaneous tracking performance was consistent across materials with low to high moduli. Thus, DoPIo may benefit from simultaneously tracking ARFI displacements using different focal configurations.

Intra-beam Scatterer Localization for Speckle Bias Correction

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Background: Lateral phase estimation methods, including transverse oscillation and spatial quadrature, have been previously developed to image lateral flow. In this work, we use a similar technique to estimate a scatterer's lateral position relative to the centerline of a focused beam, to be used in speckle bias error correction in ARFI-induced tissue displacement tracking.

Methods: A custom algorithm based on the quadrature data and the relationship between analytically derived lateral beam profiles for three different receive apodizations (uniform positive, single-cycle antisymmetric, and two-cycle antisymmetric) was implemented to estimate a scatterer's lateral location across both the main and side lobes of the beam. A 128-element L11-5v array (*fc* = 7.5MHz, 65% bandwidth, pitch = 0.3mm) was modeled in Field II, and single-point-scatterer simulations with uniform positive transmit apodization and the different receive apodizations were run for F/# = 1.0, 1.5, and 2.0. Errors between the estimated and known lateral location of the scatterer were mapped laterally and ±2λ axially about each focal point.

Results and conclusion: For each F/#, the error in the estimated scatterer position within the -10 dB width of the main lobe was determined to be ≤ 12% of the -10 dB beam width; the error within the -20 dB width of the main lobe was determined to be ≤ 14% of the -20 dB beam width. The scatterer-position error peaked in the region between the main and side lobes, and the error was higher within the side lobes than the main lobe in general. These results show the potential to determine the lateral offset of speckle signals from the assumed scan line position and correct for speckle bias error in displacement tracking methods, with future work needed to refine and improve the accuracy of the algorithm and apply it in ARFI-based imaging.