BI-I01

Blood Mimicking Fluid (BMF) Properties Using Doppler Ultrasound Applications

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Doppler imaging ultrasound characterization and standardization require mimicking blood that called blood-mimicking fluid (BMF) for the exam aim of ultrasonic apparatuses, with recognized internal properties, acoustic and physical features of this artificial blood. Both acoustical and Physical merits set in the International Electrotechnical Commission (IEC) scale are determined as regular values, where the components utilized in the artificial blood preparation must have values identical to the IEC values. An artificial blood is commercially available in the medical application, may not be suitable in the mode of ultrasonic device or for rate of new imaging technique. It is sometimes qualified to have the strength to produce sound features and simulate blood configuration for particular implementations. In the current review article, appropriate artificial blood components, fluids, and measurements are described that have been created by using varied materials and process that have modified for medical applications.

Keywords: Blood Mimicking Fluid (BMF), International Electrotechnical Commission (IEC), Doppler ultrasound, Physical properties, and acoustical properties.

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BI-S01

Vector Flow Imaging Using Speckle-tracking-based Correlation-weighted Least Squares

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Vector flow imaging (VFI) has received considerable interest because the flow direction can be quantified in two or three dimensions, which overcomes conventional angle-dependent color Doppler. Many approaches have been studied such as techniques using multi-angle beams, speckle tracking (ST), and lateral oscillation. Particularly, multi-angle Doppler estimators with ultrafast plane-wave imaging are of interest, where axial velocity components projected on individual steered plane waves are combined to produce the velocity vector using least squares (LS). However, Doppler methods exhibit fundamental issues such as bias, ensemble-dependent variance, and aliasing. On the other hand, ST is aliasing-free, allowing high temporal-resolution VFI with fewer ensemble. However, it has two major problems: poor lateral velocity estimation due to diffraction limit, and estimation accuracy deteriorated by speckle decorrelation. Hence, in this study, we develop a robust ST-based ultrafast VFI by leveraging axial velocity estimates for each steered plane wave, and employing correlation-weighted LS to produce the reliable velocity vector estimate. Besides, by leveraging the super-resolution imaging developed in contrast-enhanced ultrasound, we propose a visualization approach capable of tracking flow particles according to estimated velocity vectors. Simulation, phantom experiments, as well as human carotid arteries were evaluated to demonstrate the feasibility of the proposed approach. It is shown that our approach outperforms conventional ST method and the LS-based multi-angle ultrafast imaging scheme in terms of bias and standard deviation.

BI-S02

The Application of Speckle Tracking to Time-intensity Analysis for Contrast-enhanced Harmonic Endoscopic Ultrasound Imaging

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Contrast-enhanced harmonic endoscopic ultrasound (CEH-EUS) is now widely used for the differential diagnosis of solid tumors because of its ability to demonstrate microvascularization of the tumors. However, most images acquired from CEH-EUS are interpreted subjectively. In this presentation, we will introduce a time-intensity curve (TIC) acquisition system from dynamic CEH-EUS images to provide an objective and quantitative interpretation of tumor microvascularization.

The basic technique we used in this system is speckle tracking of a region of interest (ROI) in B-mode. Speckle is a common phenomenon in coherent imaging systems. It comes from the coherent interference of scatterers, and it appears as a granular structure superimposed on the image. It is an artifact degrading target visibility and does not represent any inherent tissue properties. On the other hand, it can be used to track tissue motion. The process of speckling tracking composes of searching and matching processes. In this system, we use full search for the searching process and normalization cross-correlation for the matching process.

The algorithm for getting TICs in this system includes the following steps: 1) Circling the ROI in the B-mode (2) Performing speckle tracking the ROI in the B-mode (3) Simultaneously obtaining the intensity of ROI (the mean pixel values in the ROI) in the corresponding contrast-enhanced harmonic image (4) Outputting TICs after subtraction of the baseline intensity (for eliminating the different baseline intensities caused by other settings). Through this process, we successfully demonstrate different TIC patterns from different kinds of solid tumors. The model may provide diagnostic value clinically by providing an objective interpretation of CEH-EUS images.

BI-S03

Vortex Ultrasound in Theranostics

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Spatially concentrating and manipulating biotherapeutic agents within the circulatory system is a longstanding challenge in medical applications due to the high velocity of blood flow, which greatly limits drug leakage and retention of the drug in the targeted region. To circumvent the disadvantages of current methods for systemic drug delivery, we propose tornado-inspired acoustic vortex tweezer (AVT) that generates net forces for noninvasive intravascular trapping of lipid-shelled gaseous microbubbles (MBs). MBs are used in a diverse range of medical applications, including as ultrasound contrast agents, for permeabilizing vessels, and as drug/gene carriers. We demonstrate that AVT can be used to successfully trap MBs and increase their local concentration in both static and flow conditions. For example, we developed a functional sonography guided acoustic vortex tweezer (AVT) system to increase the local concentration of thrombolytic drugs for theranostic thrombolysis. The AVT will concentrate thrombolytic agents (tPA)-loaded microbubbles (tPA-MBs) within thrombosed vessels. In the meantime, the concentration and location of tPA-MBs can be monitored by plan wave ultrafast sonography imaging. Subsequently, these tPA-MBs can be triggered to release tPA drugs and to generate microstreaming at thrombosis area by low frequency ultrasound, improving the efficiency of thrombolysis. Since the AVT and tPA-MBs will generate shear waves in the thrombus during treatment, these shear waves can be used to generate elastic images of the thrombus for estimating the distribution of softness and hardness, thereby achieving real-time therapeutic purpose. The proposed AVT technique is a compact, easy-to-use, and biocompatible method that enables systemic drug administration with extremely low doses.

BI-S04

Molecular Mechanisms of Ultrasound-mediated Microbubble Cavitation for Enhancing the Permeability of Human Keratinocytes and Skin

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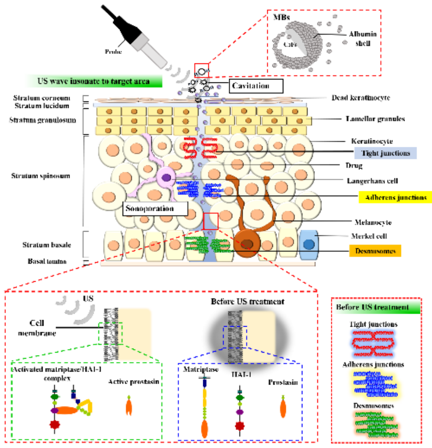
We have previously reported that ultrasound (US)-mediated microbubble (MB) cavitation (US-MB) changed the permeability of the skin and significantly enhanced transdermal drug delivery (TDD) without changing the structure of the skin. In this study we found that US-MB enhanced TDD via disruption of epidermal cell–cell junctions and increased matriptase activity. Matriptase is a membrane-bound serine protease regulated by its inhibitor hepatocyte growth factor activator inhibitor-1 (HAI-1), and it is expressed in most epithelial tissues under physiologic conditions. Matriptase is expressed in mice after chronic exposure to UV radiation. This study found that US-MB can be used to monitor active matriptase, which rapidly formed the canonical 120-kDa matriptase-HAI-1 complex. These processes were observed in HaCaT human keratinocytes when matriptase activation was induced by US-MB. This study firstly found that US-MBs cavitation transiently changes the structure of the desmosomes to monitor active matriptase in human skin. The active matriptase complex can be detected from 10 min to 3 hours after US-MB from the basal layer to the granular layer and gradually decaying from 6 to 12 hours. The activated prostasin was observed in the uppermost layer after 3 hours, then faded thereafter. Different degrees of cavitational TDD enhancement are associated with various levels of matriptase and prostasin activation. The average cell-to-cell distance increased after 3 hours and then decreased to the original cell-to-cell distance.



BI-S05

Technological Review and Clinical Application Strategy of Focused Ultrasound Induced Blood-Brain Barrier Opening

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In this presentation, the focused ultrasound induced blood-brain barrier (BBB) opening technology is reviewed. The materials consist the review identifying threshold of cavitation-based manipulation for BBBo. To translate BBBo for wider clinical use, a greater understanding of BBBo threshold, monitoring indicators of BBBo, and means to control BBBo stability are needed. BBBo threshold increases with higher frequencies. Critical parameters including the exposure level and microbubble concentration, are about to be summarized and reviewed. Passive cavitation detection to monitor cavitation showed that sub-harmonics can be used as a metric to control BBBo. BBBo based on PCD-feedback control using sub-harmonics, harmonics, and ultra-harmonics is in development, which can be done without MRI. At last, different types of guiding approaches as well as strategies been adopted in clinical practice will be introduced.

BI-S06

High Frequency Ultrasound Blood Flow Imaging for Human Hand Tendon

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Objective: Neovascularization of injury tendons has been shown to be correlated with pain degree. A follow-up investigation of clinical hand tendon rupture and the correlation between neovascularization and subject recovery level is necessary for accurate diagnosis of the condition and optimal diagnosis. Usually due to the limitations of the clinical ultrasound system, neovascularization can only be measured within the injured Achilles tendon.

Methods: High-frequency micro-Doppler based on curvilinear structure enhanced imaging was used to verify the algorithm in the microvasculature of mice kidney and spleen. Subsequently, a follow-up investigation was conducted on 5 subjects with different rehabilitation periods but also tendon rupture injuries.

Results: In animal study: Using a 40 MHZ ultrasound transducer, the microvasculature of mice kidney and spleen can be seen at 9 mm in depth. Compared image quality with other blood flow imaging algorithm, better contrast-to-noise ratio (CNR) and signal-to-noise ratio (SNR) are obtained, in the case of without the use of ultrasound contrast agents, can determine the smallest blood vessels diameter of 35 μm. In human studies, the neovascular density of injured hand decreased significantly in the subjects 1,2,4 and 5who had sustained recovery for less than 5 months. And there was no significant difference in neovascularization density between the injured and healthy hands of subject 3 after approximately 12 months of continuous rehabilitation. The results of the high-frequency ultrasound assessment were similar to those of the subject's hand function parameters as assessed by professionals in the Physical Medicine and Rehabilitation department of National Cheng Kung University Hospital (Tainan, Taiwan).

Conclusion: The results of human study show that micro-Doppler can successfully measure the neovascularization of the injured tendon and the possibility of the recovery degree of the subject based on the curvilinear structure enhanced imaging technique, and may be used as a diagnostic tool for tendon injury in clinical practice.

BI-S07

Functional Ultrasound Neuro-imaging: Insights into Ischemic Stroke

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Functional ultrasound (fUS), based on Ultrafast Doppler imaging, is an ultrasensitive and quantitative microvascular imaging technique that is able to access hemodynamics of brain and neurovascular coupling, expanding the field of application of ultrasound imaging to brain researches. Stroke is one of the most severe and devastating neurological diseases in the world. In terms of different cerebrovascular environment after stroke including the occluded level, reperfusion status and collateral abundance majorly determines the tissue fate from irreversible damage to salvageable condition in the brain. In this research, fUS was conducted to real-time monitor the hemodynamic response during ischemic stroke in photothrombotic (PT) rat model. With high frequency ultrasound, it can provide high spatiotemporal Doppler imaging (<100 μm, <1ms) to monitor perfusion change, even arterioles and venules within whole brain of small animals.

BI-P01

Deep Learning for Automatic Segmentation of Synovium on Wrist Ultrasound Images

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Background: Synovitis is the main feature of rheumatoid arthritis (RA). In clinical practice, the severity of sonographic synovitis is scored (0-3) using OMERACT criteria by physician reading but this approach is only semi-quantitative. Computer-aided quantitative image analysis is more accurate in assessing the severity of synovitis but manual delineation of synovium border brings inconvenience. In this study we develop an artificial intelligence based method for automatic segmentation of synovium on wrist ultrasound images.

Methods: Images were obtained with standard long-axis scanning of dorsal wrists in RA patients by an ultrasound equipment (Philips iu22 equipped with a 12 MHz linear transducer) and were digitally stored in PNG format in a database. All images were resized to 303*781*3. The extent of synovium was labeled by an experienced rheumatologist. A convolutional neural network, U-net model, using python language and Keras application programming interface was adopted for deep learning. The parameters for training included learning rate 0.00001, batch size 100, epoch 128 and Adam optimizer. The prediction performance was assessed using Dice coefficient.

Results: There were 8304 images for training and 500 images for validation. The mean Dice was 0.842 ± 0.085 (range 0.496-0.969). Of validation images, 376 images (75.2%) had a good prediction (Dice ≥0.8), 92 images (18.4%) had a fair prediction (Dice 0.7- <0.8) and 32 images (6.4%) had a poor prediction (Dice <0.7).

Conclusion: This trained U-net model is the first artificial intelligence based method found in the literature for automatic segmentation of synovium on wrist ultrasound images. It had a good prediction performance and has the potential for clinical use.

Keywords: deep learning; segmentation; synovium; rheumatoid arthritis; ultrasound.