Guest Editorial
Introduction to the Special Issue on Recent Advances in Ultrasound Technology for Brain Imaging and Therapy

THE emergence of new technologies has dramatically accelerated our understanding of the human brain function. Over the past decade, ultrasound has become a valuable tool in preclinical animal studies and clinical practice in many areas of the brain. This is because it can not only provide information about the structure and function of brain tissues but also constitute a potential treatment tool for brain disease. The recent FDA approval and success of ultrasound ablation techniques for essential tremors is an example of how ultrasound can revolutionize clinical practice. Similarly, recent brain ultrasound advances such as noninvasive blood–brain barrier (BBB) opening, ultrasound neuromodulation, and functional brain imaging have great potential to improve human patient outcomes in neurology and neurosurgery. Ultrasound is thus expected to play an increasingly important role in the diagnosis and treatment of brain disease in the upcoming years.

This Special Issue, "Recent Advances in Ultrasound Technology for Brain Imaging and Therapy," highlights a selection of the state-of-the-art techniques relevant to studying and treating the brain. The 20 papers included in this Special Issue cover a wide range of topics related to brain applications, including ultrasound neuromodulation, brain imaging, skull assessment and compensation, passive brain mapping, and transducer and system.

The Editorial Team of this Special Issue has composed a review paper, which introduces the latest research on brain ultrasound and basic knowledge of brain ultrasound, including the acoustic properties of the brain/skull and engineering of ultrasound techniques.

Ultrasound neuromodulation is an emerging technique that can noninvasively modulate the neural activities in the targeted brain regions. It has the advantages of noninvasiveness and the ability to target deep brain regions with high spatial resolution, which has attracted great attention in the field of brain applications. There are five papers in the Special Issue talking about neuromodulation. Lu *et al.* have reported ultrasound can successfully evoke neural activities in the visual cortex and can be used as a new tool for noninvasive cortical visual prosthesis. Pang *et al.* assessed ultrasound stimulation to modulate the hypothalamus, which may provide a new method for controlling aging. Wang *et al.* demonstrated that ultrasound may have neuromodulatory effects on innate defensive behaviors in small animals, and LIFU may be used as a novel tool for the treatment of psychological diseases associated with defensive behaviors. Huang *et al.* have demonstrated that ultrasound can be a safe and capable tool for activating neuronal autophagy in small animals. Schafer *et al.* describe a low-intensity-focused ultrasound (LIFU) stimulation system for noninvasive neuromodulation.

Skull is still the major obstacle for brain ultrasound in clinical study because of its deleterious effects including attenuation, aberration, refraction, and mode conversion. The accurate assessment and compensation of the effects of the skull are very important for brain ultrasound. Murashima *et al.* investigate the anisotropic longitudinal wave propagation in swine skulls. Jiang *et al.* presented a spectrum-domain, full-matrix phase shift migration method to correct the phase distortion for transcranial ultrasound imaging. Mozaffarzadeh *et al.* presented a method for estimating the speed of sound and an adaptive beamforming technique for phase aberration correction in a skull mimicking model.

The skull influence can be ignored when brain ultrasound is applied in neonates and in open skull studies. High temporal–spatial resolution ultrasound brain imaging can be achieved for these applications. Jakovljevic *et al.* proposed an angular coherence-based beamforming method that suppresses incoherent noise and motion artifacts to improve the detection of small blood flow in the neonatal brain.

New developments in ultrasound transducer and system are enabling new ranges of diagnostics and therapy for the brain using ultrasound. Estrada *et al.* presented a new spherical array for transcranial delivery of focused ultrasound and 3-D optoacoustic tomography of the rodent brain. The array provides a promising method for 3-D image-guided neuromodulation and targeted BBB opening to therapeutic ultrasound interventions. Wu *et al.* described a transducer that can be rotated according to the different geometric shapes of the skull so that the efficiency of the ultrasonic penetration can be improved, and Rahimi *et al.* a 3.3-MHz spherically curved phased array for transcranial focused ultrasound delivery in small animals. Zhou *et al.* reported on a method capable of clock synchronization using an optical fiber, and the proposed clock scheme is suitable for a magnetic resonance imaging (MRI)-guided large-scale ultrasound array system.

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Cueto *et al.* designed a spatial response identification algorithm for ultrasound transducer calibration and modeling for brain imaging applications. Choi *et al.* described a focused ultrasound stereotactic targeting method for various brain applications.

Passive acoustic mapping enables spatiotemporal monitoring of cavitation during focused ultrasound brain therapeutics. This technique can monitor therapeutic ultrasound procedures to confirm the spatial distribution and amount of induced cavitation activity. Kamimura *et al.* implemented a GPU-accelerated sparse matrix-based beamforming for spatiotemporal monitoring of cavitation with circulating microbubbles during the ultrasound brain therapy. Davies *et al.* described an algorithm that can locate acoustic sources with an improved spatial resolution, which could be used to target and monitor drug delivery into the brain.

Other interesting contributions in brain ultrasound include the work by Hosseini *et al.* who proposed a sectored-multiring ultrasonic transducer capable of focusing the ultrasonic waves for powering dust implants at different depths and regions of the brain, and Chandrasekaran *et al.* reporting a generalization of the impedance flow method that could accurately capture the complex brain motion that occurs during a traumatic impact.

The Editors also wish to mention several contributions who made this Special Issue possible. Special thanks go to our Editors-in-Chief, Prof. Peter Lewin and Prof. Steven Freear, for their invaluable and tireless support in promoting this Special Issue. Thanks also go to the transaction officers Natalie Cicero and Eileen McGuinness for the organization. The Editors are grateful to the authors who contributed to this Special Issue and to the Associate Editors who organized the peer-review process and, more importantly, to all the anonymous reviewers who shared their time and effort in providing their valuable comments.

Finally, as ultrasound researchers, we wish to welcome additional scientists and engineers to join in on brain applications and help to develop new technologies to help patients, and ultimately improve human lives.

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