# The Ever-Growing Field of High-Frequency Biomedical Ultrasound

COMPARED with other medical imaging counterparts, ultrasound has advantages owing to its real-time imaging capability, easy access, and cost-effectiveness. High-frequency (>20 MHz) ultrasound has been developed over the last few decades and is attractive because it provides high-resolution medical imaging and ultrasound backscattering microscopy (UBM) measurements, with applications targeting small animal imaging and some areas of human diagnosis. In recent years, driven by growing needs in intravascular ultrasound (IVUS) imaging, minimally invasive surgery, and particle manipulation, high-frequency ultrasound has continued to flourish as a niche modality and has expanded its important role in both diagnostic imaging and therapy. Concomitant needs have thus arisen in technological research and development to innovate materials, devices, algorithms, and systems for a variety of high-frequency ultrasound applications in medicine and biology.

To highlight the latest advances in high-frequency biomedical ultrasound technology and applications, the IEEE TRANSACTIONS ON ULTRASONICS, FERROELECTRICS, AND FREQUENCY CONTROL (TUFFC) have prepared a Spotlight Issue on the theme of "High-Frequency Ultrasound for Biomedical Applications." Over a 7-month period, we have compiled a collection of 17 review articles and original research papers on various aspects of high-frequency ultrasound technology. This Spotlight Issue serves well as a resource point for researchers to disseminate and learn about the latest clinical and technological advances in high-frequency ultrasound.

High-frequency ultrasound imaging is actively being applied to multiple clinical domains. In [A1], Huang *et al.* have demonstrated that high spatiotemporal resolution visualization of myocardial strains in small animals may be achieved through vector Doppler estimation. Also, in [A2], Tsai *et al.* have reported that high-frequency ultrasound elastography is useful for assessing the elastic properties of skin and scars. In addition, the investigation reported by Wang *et al.* [A3] is the latest example of realizing endoscopic imaging using high-frequency ultrasound.

The development of new therapeutic applications using high-frequency ultrasound, including cellular manipulation, is a highlight of this Spotlight Issue. In [A4], Zeng *et al.* have presented how high-frequency ultrasound beams can be used to manipulate and mechanically deform leukemia cells. In [A5], Balasubramanian *et al.* have reported using GHz ultrasound and electrode chip-scale arrays to stimulate and influence the morphology of human neural cells. In [A6], Silverman *et al.* have found that high-frequency ultrasound can be used to activate perfluorocarbon nanodroplets for the treatment of glaucoma. In [A7], Wu *et al.* have demonstrated a dual-mode ultrasound catheter for ultrasound-guided intravascular sonothrombolysis *in vitro*.

As the core device for high-frequency ultrasound, new transducer materials, fabrication, and characterization have been presented in several review and research papers. In [A8], Chen *et al.* have reviewed high-frequency ultrasound transducers for photoacoustic imaging. In [A9], Luo *et al.* have showcased a new broadband high-frequency transducer that enabled functional photoacoustic microscopy for psoriasis progression. In [A10], He *et al.* have demonstrated the use of a piezo-driven single-element transducer to achieve 3-D high-frequency ultrasound imaging. In [A11], Che *et al.* have presented the development of a high-frequency micro-convex array for small animal imaging. In [A12], Zhao *et al.* have described how to devise an ultrawide-bandwidth, high-frequency transducer with a gradient acoustic impedance matching layer. In [A13], Kim *et al.* have presented the design of a new miniaturized IVUS transducer with a highly attenuative backing layer.

New systems and hardware for high-frequency ultrasound imaging are continuously being developed. For instance, Kong *et al.* [A14] have shown how an integrated US-OPT-NIRF tri-modality imaging system can be devised. Also, in [A15], Li *et al.* have reported the design of echo signal receiving and data conversion integrated circuits for portable high-frequency ultrasound imaging systems. In parallel to these system development efforts, various signal processing algorithms related to high-frequency ultrasound are being devised by many laboratories. In this Spotlight Issue, Jokerst *et al.* [A16] have described how RF data can be synchronized for high-accuracy, high-resolution photoacoustic tomography. As well, in [A17], Kang *et al.* have reported a new sub-Nyquist sampling method for high-frequency ultrasound imaging.

Readers may have found out through reading this Spotlight Issue that many of the recent high-frequency ultrasound research investigations are built upon the pioneering works of outstanding contributors to this field, namely, Prof. Stuart Foster of the University of Toronto, Toronto, ON, Canada, and Prof. K. Kirk Shung, previously from Pennsylvania State University, State College, PA, USA, and then at the University of Southern California, Los Angeles, CA, USA. Both have recently retired from their academic positions, but they remain active in our community as mentors for the new generation of high-frequency ultrasound researchers. The UFFC TRANSACTIONS hereby pay tribute to these

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pioneers for their significant contributions to the field of high-frequency biomedical ultrasound.

The Guest Editors would like to take this opportunity to thank all contributing authors for their excellent work. The Guest Editors hope this Spotlight Issue can serve to prompt further engineering innovations and clinical translation endeavors in high-frequency biomedical ultrasound.

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## APPENDIX: RELATED ARTICLES

[A1] H. Huang, W.-T. Chang, and C.-C. Huang, "High-spatiotemporal-resolution visualization of myocardial strains through vector Doppler estimation: A small-animal study," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1859–1870, Jun. 2022, doi: 10.1109/TUFFC.2022.3148873.

[A2] W.-Y. Tsai, Y.-Y. Hsueh, P.-Y. Chen, K.-S. Hung, and C.-C. Huang, "High-frequency ultrasound elastography for assessing elastic properties of skin and scars," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1871–1880, Jun. 2022, doi: 10.1109/TUFFC.2022.3154235.

[A3] N. Wang *et al.*, "High-frequency endoscopic ultrasound imaging with phase-corrected-and-sum and coherence factor weighting," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1881–1888, Jun. 2022, doi: 10.1109/TUFFC.2022.3142250.

[A4] Y. Zeng *et al.*, "Manipulation and mechanical deformation of leukemia cells by high-frequency ultrasound single beam," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1889–1897, Jun. 2022, doi: 10.1109/TUFFC.2022.3170074.

[A5] P. S. Balasubramanian and A. Lal, "GHz ultrasound and electrode chip-scale arrays stimulate and influence morphology of human neural cells," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1898–1908, Jun. 2022, doi: 10.1109/TUFFC.2022.3152427.

[A6] R. H. Silverman, R. Urs, M. Burgess, J. A. Ketterling, and G. Tezel, "High-frequency ultrasound activation of perfluorocarbon nanodroplets for treatment of glaucoma," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1910–1916, Jun. 2022, doi: 10.1109/TUFFC.2022.3142679.

[A7] H. Wu, B. Zhang, C.-C. Huang, C. Peng, Q. Zhou, and X. Jiang, "Ultrasound-guided intravascular sonothrombolysis with a dual mode ultrasound catheter: *In-vitro* study," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1917–1925, Jun. 2022, doi: 10.1109/TUFFC.2022.3153929.

[A8] D. Ren, C. Li, J. Shi, and R. Chen, "A review of high-frequency ultrasonic transducers for photoacoustic imaging applications," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1848–1858, Jun. 2022, doi: 10.1109/TUFFC.2021.3138158.

[A9] X. Luo *et al.*, "Broadband high-frequency ultrasonic transducer based functional photoacoustic mesoscopy for psoriasis progression," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1926–1931, Jun. 2022, doi: 10.1109/TUFFC.2021.3136870.

[A10] L. He, B. Wang, Z. Wen, X. Li, and D. Wu, "3-D high frequency ultrasound imaging by piezo-driving a single-element transducer," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1932–1942, Jun. 2022, doi: 10.1109/TUFFC.2022.3145162.

[A11] W. Chen *et al.*, "Design and fabrication of a high-frequency microconvex array transducer for small animals imaging," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1943–1951, Jun. 2022, doi: 10.1109/TUFFC.2022.3146309.

[A12] J. Zhao *et al.*, "Ultrawide bandwidth high-frequency ultrasonic transducers with gradient acoustic impedance matching layer for biomedical imaging," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1952–1959, Jun. 2022, doi: 10.1109/TUFFC.2022.3141203.

[A13] H. Kim *et al.*, "High-attenuation backing layer for miniaturized ultrasound imaging transducer," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1960–1969, Jun. 2022, doi: 10.1109/TUFFC.2022.3164451.

[A14] R. Kong *et al.*, "Integrated US-OCT-NIRF tri-modality endoscopic imaging system for pancreaticobiliary duct imaging," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1970–1979, Jun. 2022, doi: 10.1109/TUFFC.2022.3164777.

[A15] D. Li *et al.*, "Echo signal receiving and data conversion integrated circuits for portable high-frequency ultrasonic imaging system," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1980–1993, Jun. 2022, doi: 10.1109/TUFFC.2022.3161293.

[A16] L. Fu *et al.*, "Synchronization of RF data in ultrasound open platforms (UOPs) for high-accuracy and high-resolution photoacoustic tomography using the 'Scissors' programming method," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 1994–2000, Jun. 2022, doi: 10.1109/TUFFC.2022.3164371.

[A17] J. Kang, H. Yoon, C. Yoon, and S. Y. Emelianov, "High-frequency ultrasound imaging with sub-Nyquist sampling," *IEEE Trans. Ultrason., Ferroelectr., Freq. Control*, vol. 69, no. 6, pp. 2001–2009, Jun. 2022, doi: 10.1109/TUFFC.2022.3167726.

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