Wearable ultrasound bioelectronics for healthcare monitoring

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Received: May 12, 2023; Accepted: May 22, 2023; Published Online: May 24, 2023; https://doi.org/10.1016/j.xinn.2023.100447

Citation: Jiang S., Zhang T., Zhou Y., et al., (2023). Wearable ultrasound bioelectronics for healthcare monitoring. The Innovation **4(4)**, 100447.

Customized and personalized healthcare, being self-administered by patients, is highly sought after in light of the increasing burdens of chronic illnesses and aging populations. Outside clinics that empower individuals to have a more prominent role in managing their health are becoming a trend due to many benefits. For example, they can reduce hospital visits and infection risk during a pandemic like COVID-19. Flexible bioelectronics, which can be mounted onto skin, attached to clothing, and even implanted into bodies (e.g., epidermal electronics, wearable electronics, and implantable electronics) are ideal candidates for this purpose.[1] Different from conventional medical instruments in hospitals that are usually bulky, non-portable, mono-functional, and time-consuming,[2] flexible bioelectronics enable continuous, non-invasive, real-time, and comfortable monitoring of vital physiological signals, offering clinically related information for disease diagnosis, preventive healthcare, and rehabilitation care. This technology holds great promise for tracking and managing chronic conditions such as cardiovascular problems, metabolic disorders, and diabetes, which is of great significance in a rapidly aging population. Moreover, flexible bioelectronics are ultrathin, low-modulus, and lightweight, rendering them “mechanically invisible” to objects with arbitrary surfaces. Fueled by the rapid development of materials and manufacturing technologies, an era of flexible, wearable, and conformal devices is above the horizon.

Based on the working mechanisms, flexible bioelectronics nowadays can be classified into three categories[2,3]: (1) flexible mechanical bioelectronics, which utilize their own mechanical deformation to realize measurements, for example, flexible strain or pressure sensors for human motion monitoring; (2) flexible light bioelectronics, which rely on light-matter interaction to deliver biometric information, for example, flexible photonic skin for non-invasive molecular sensitivity; and (3) flexible sound bioelectronics, which exploit sound-matter interaction, for example, wearable ultrasound imager for cardiac imaging. Among these, flexible mechanical bioelectronics are the most frequently utilized, as the contact interaction approach is the simplest and most straightforward. Comparatively,

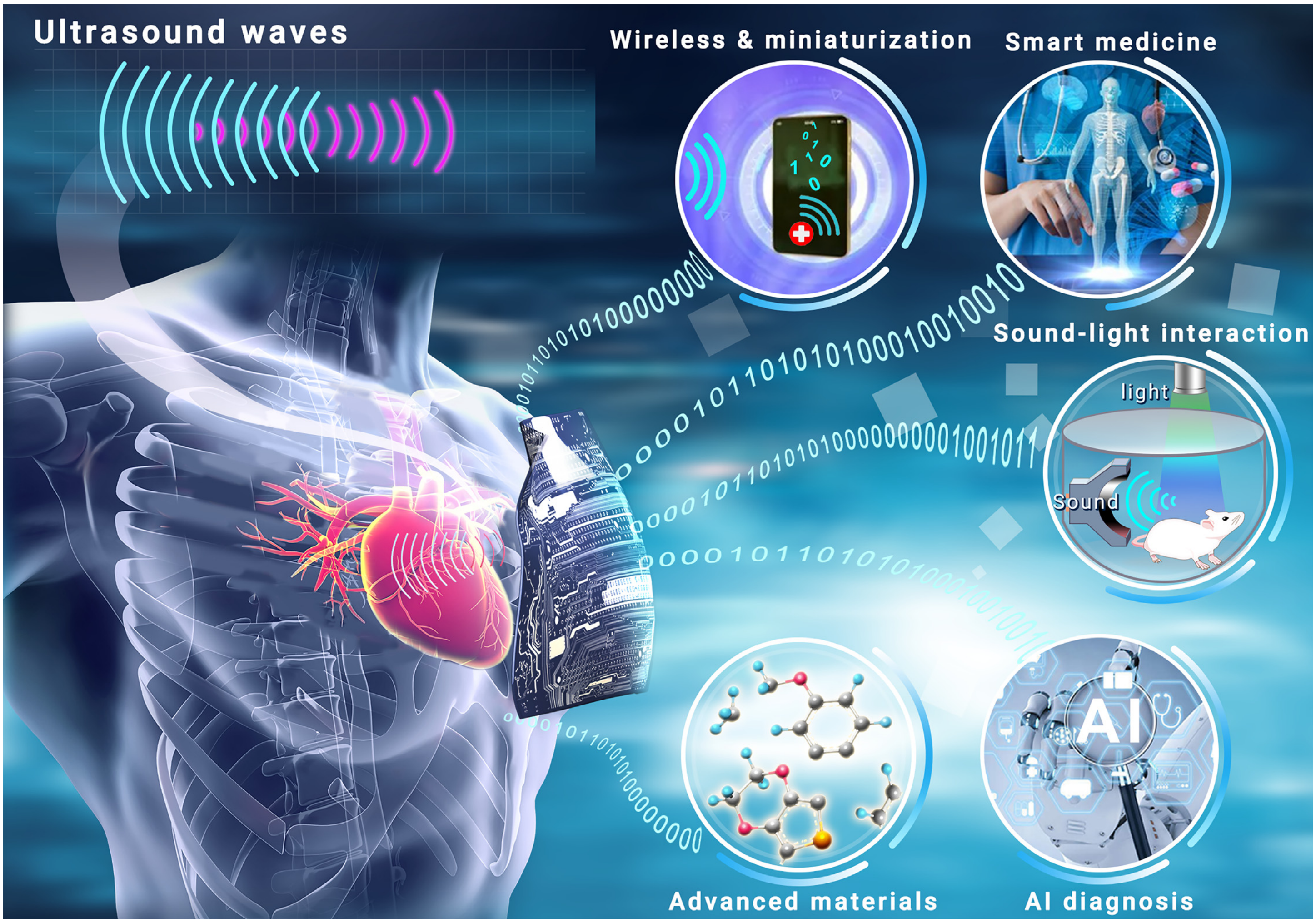

Figure 1. The concept of wearable ultrasound bioelectronics for noninvasive, real-time, continuous, and comfortable monitoring of vital physiological signals. Further efforts include miniaturization, wireless data transmission, smart medicine, sound-light interaction (such as photoacoustic imaging and acousto-optic imaging), AI diagnosis, advanced materials, and other related improvements.

flexible light bioelectronics have the advantages in aspects of non-invasiveness, low hysteresis, high sensitivity, insusceptibility to electromagnetic interference, and large capacity for multiplexing. However, their clinical applications are limited by the finite wavelength-dependent light-penetration depth. The emerging flexible sound bioelectronics have the potential to overcome these limitations, as they offer non-invasiveness, low power consumption, miniaturization, sufficient penetration depth, and high spatial resolution.[2]

Recently, the potential of flexible sound bioelectronics, especially flexible ultrasound bioelectronics, has garnered significant interest. Several impressive achievements in this infant field are emerging, such as a bioadhesive ultrasound imager capable of long-term continuous imaging of diverse organs[4] and an intrinsically stretchable ultrasound imager for cardiac imaging.[5] They are the most representative and showcasing works so far, displaying two different developmental pathways. The former ultrasound imager consists of a thin and rigid ultrasound probe adhered to the skin via a couplant made of a soft, tough, antidehydrating, and bioadhesive hydrogel-elastomer hybrid. It emphasizes the bioadhesive couplant rather than the biodevice itself. The rigid ultrasound probe enables high density of element arrays (400 elements per square centimeter), high imaging resolution, multifunctionality for different internal organs (e.g., blood vessels, muscle, heart, gastrointestinal tract, and lung), stable imaging quality even during dynamic body movements, and robust reliability in long-term, continuous (48 hours) applications. However, the primary challenges of this type of ultrasound imager remain the wearing discomfort and the material characteristics (including electrical, optical, thermal, chemical, and acoustic properties) of the bioadhesive couplants.

In comparison, the latter intrinsically stretchable ultrasound imager follows the current trend of making biodevices thin and stretchable for conformal attachment to the body. It features piezoelectric transducer arrays, liquid metal composite electrodes, and triblock copolymer encapsulation. The entire device has a low Young's modulus of 921 kPa and a high stretchability of up to approximately 110%, while the Young's modulus and stretchability of the skin are about 1 MPa and 20%, respectively. The imaging performance (as measured by spatial resolution, signal-to-noise ratio, location accuracy, dynamic range, and contrast-to-noise ratio), combined with capabilities of echocardiography from several views, monitoring during motion, and automatic image processing, provides a heuristic paradigm for the wearable ultrasound imager. However, despite advances in mechanical flexibility, the applications of intrinsically stretchable materials are still strictly limited due to a lack of stability and reliability, which means that it is unable to provide the comparable high performance as conventional, stiff, non-stretchable probes. Specifically, the stretchable ultrasound imager still suffers limitations of low imaging resolution, unstable imaging quality during body motions, short continuous imaging duration, susceptibility to external disturbance, and liable to device failure.

Achieving both functionality and convenience is vital toward practical applications, and a number of technological challenges and research opportunities that lay ahead need to be addressed (Figure 1). Initially, the currently available studies primarily concentrate on the design and production of probes, which rely on an extensive, wired, and external data acquisition system. Future endeavors need to prioritize wireless systems, miniaturization, and integration. For instance, the data acquisition system can be scaled down to the size of a mobile phone. Second, in addition to ultrasound imaging, research can also be extended to hybrid imaging of sound and light, such as photoacoustic/optoacoustic imaging, which can provide additional structural and functional information of high resolution to improve the probing of complex environments and hence expand the scope of applications. Furthermore, comparable functions based on different mechanisms can verify each other, avoiding potential false positives or false negatives and thus improving the robustness of the system. Third, advanced imaging algorithms are conducive to accommodating the phase distortion and therefore image artifacts originating from the non-planar and dynamic chest. This is essential to improving imaging resolution, especially for deep-seated organs. Fourth, many demonstrated functionalities and device prototypes in this field are still in their infancy and are mostly limited to laboratory research, or sometimes solely for demonstrations under ideal assumptions, without considering real-life environment. Clinical-grade imaging metrics of various internal organs should be taken into account. Fifth, flexible bioelectronics embrace an almost ideal platform to realize AI-assisted diagnosis, with a tremendous amount of data being provided to the machine learning algorithms and training datasets. It would be exciting to develop an AI-assisted healthcare system like GPT-4. Sixth, micro-/nano-scale high-precision fabrication techniques are prerequisite. Many of the currently available techniques are still in their early stages, such as liquid-based printing, laser-based techniques, and lithography (e.g., photo- and two-photon), and recent fashionable 4D printing. Last but not least, the development of flexible bioelectronics substantially relies on the exploration and maturation of advanced materials. However, in the field of flexible bioelectronics, while the majority of works involve mechanical, electrical, and photoelectric properties of materials, few works pay attention to the acoustic properties of materials.

As a highly interdisciplinary research, wearable ultrasound bioelectronics exhibit inherent complexity and diversity. The realization of such devices necessitates extensive and in-depth cooperation of researchers and practitioners from across all related disciplines, including materials, chemistry, physics, mechanics, algorithms, software, hardware, clinical medicine, and more. However, different disciplines inevitably show divergent characteristics. The already reported wearable ultrasound devices are just the tip of the iceberg, and great potential in this emerging field is waiting to be explored. Conceptual breakthroughs, multidisciplinary research, and demand-driven innovative applications are the key to future work. If the current growth trend in wearable ultrasound research continues, it is not inconceivable for the field to witness a near-explosion in academic and industrial interest. Such an outcome was witnessed over the last decade in the field of flexible mechanical bioelectronics and more recently in the closer field of flexible light bioelectronics. Flexible sound bioelectronics appear to be next.

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ACKNOWLEDGMENTS

This work was supported by the National High Level Hospital Clinical Research Funding (Grant No. 2023-GSP-QN-23), the National Natural Science Foundation of China (Grant No. 52105575), the Fundamental Research Funds for the Central Universities (Grant No. QTZX23063), and the Proof of Concept Foundation of Xidian University Hangzhou Institute of Technology (Grant No. GNYZ2023YL0302).

DECLARATION OF INTERESTS

The authors declare no competing interests.