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In recent years, less invasive medical treatments are desired, and various minimally invasive and noninvasive therapeutic devices and methods have been developed. The same is true for drugs, development of therapeutic agents with few side effects and high effectiveness is an urgent issue. Taking into consideration the recent population aging, in addition to extending the life expectancy, there is also a high demand for development of various therapeutic methods and drugs suitable for various medical conditions.

Ultrasound has already been widely used as a diagnostic method, and with advancement of nonlinear acoustics and progress of medical-engineering collaboration, sophistication as a diagnosis or treatment method is attempted. Ultrasound imaging is a diagnostic method that is simple and real-time superior to other modalities such as X-ray CT and MRI and is used widely. In addition, in terms of the spatial resolution, great improvements are also achieved due to sophistication of the imaging technique, use of micro-bubbles as contrast agents. Ultrasound is also applied in therapeutic purpose. HIFU (high intensity focused ultrasound) is applied for such therapeutic ultrasound. In the treatment using focused ultrasound, it is possible to treat the affected part noninvasively and selectively by focusing ultrasound irradiated from the outside of the body. Ultrasound energy is absorbed by living tissue and turns into heat, and tissues such as tumor undergo thermal denaturation. Furthermore, if micro-bubbles are injected into the tumor site, the effect of heat dissipation from the bubbles can also be utilized.

In the noninvasive medical treatment combining ultrasound with appropriate pharmaceuticals, it is important to elucidate the propagation of ultrasound in living body, the oscillation of micro-bubbles, the interaction between ultrasound and living tissue. By utilizing them, a diagnostic and therapeutic integrated system using ultrasound is realized, and various treatments such as noninvasive malignant tumor treatment become possible. Hereinafter, recent research examples are shown. Heat coagulation treatment in which micro-bubbles are actively nucleated at the tumor site and the local heat conversion efficiency of ultrasound energy is enhanced. The immune system to anti-tumor is stimulated by HIFU. Cell membranes permeability is temporarily enhanced by the mechanical action of focused ultrasound. Pharmacological activating of drugs is achieved by focused ultrasound. Thrombus is lysed by ultrasound together with the drug. The concentration of drug in the affected area is increased by the breaking of the drug-containing micelles, liposomes etc. by focused ultrasound. The blood brain barrier is opened by HIFU and the drug delivery efficiency from the cerebral blood vessel to the brain tissue is increased.

On the premise that drugs and ultrasound are used together, they are regarded as combination products, and even if the drugs are approved for medical use, a new examination is required. According to the FDA (Food and Drug Administration), combination products are therapeutic and diagnostic products that combine drugs, devices, and/or biological products. Differences in regulatory pathways for each component can impact the regulatory processes for all aspects of product development and management, including preclinical testing, clinical investigation, marketing applications, manufacturing and quality control, adverse event reporting, promotion and advertising, and post-approval modifications.

Here, as a novel development of therapeutic ultrasound, we will present the prospects for developing a combination device with pharmaceuticals and others.