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Preface

Ultrasound in drug and gene delivery☆

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Fairy tale, fantasy and science fiction stories are replete with magical (or high tech) healings in which a wand or an electronic scanner is passed over an injury or illness, and the wound or infirmity is quickly and painlessly healed. No knife, no blood, and no pain—what a wonderful world it would be. Unfortunately, modern medicine has not yet caught up with our dreams of painless and non-invasive healing. However, we are making progress towards such a goal with ultrasonic drug and gene delivery, a non-invasive and painless technology that can direct therapeutic energy and release healing agents to target sites within the body.

Ultrasound (US) technology in medicine has developed rapidly over the past four decades. Although US was first used therapeutically [1], its use in diagnostic imaging commenced shortly thereafter [2] and quickly surpassed its therapeutic use in the clinic. While the concepts and applications of therapeutic use were slowly incubating, the need for non-invasive diagnostic imaging engendered the rapid development of ultrasonic technology. Now this mature technology is spreading to other medical applications, including a return to its roots of medical therapy.

In this issue, we present the current applications and future prospects of ultrasound in various aspects of drug and gene delivery. There are many advantages to ultrasound that make it ideal for the delivery of therapeutics and the stimulation of tissues—perhaps the most important of which is that US is a mechanical and yet non-invasive means of delivery that can be applied to a very wide range of therapeutics and target sites.

Another great impetus to the advancement of ultrasonic drug and gene delivery was the advent of engineered gas bubbles that were originally developed as contrast agents for imaging applications. Excitation of these bubbles by insonation leads to fluid convection, high fluid shear stresses, shock waves, free radicals, and high temperatures, all of which can produce significant biological effects, both beneficial and harmful to cells. The beneficial effects, with respect to drug and gene delivery, include the loosening of cell-to-cell junctions, the permeabilization (and even poration) of cell membranes, the stimulation of stress response (or other) pathways in cells, the release of drugs and genes from various carriers, the deposition of heat, and the activation of some chemicals by free radicals. The detrimental effects include unwanted cell injury and death, and unwanted degradation of the drugs and polynucleotides. Thus, one of the challenges to ultrasonic drug and gene delivery is to find the correct balance of ultrasonic parameters that maximizes helpful and minimizes harmful effects in order to create a functional therapeutic window.

This issue begins with two review articles that teach the physics of ultrasound itself and of the interaction of ultrasound with gas bubbles. Following this introduction are three articles that review and evaluate the technology and devices used as the therapeutic carriers or as cavitation enhancers in ultrasonic delivery. These include gas bubbles, liposomes, and nanoparticles such as micelles, emulsions, and polymeric nanoparticles. These articles on delivery technology complete the foundation of physics and chemistry for the subsequent reviews that summarize and critically analyze the application of ultrasonic-enhanced drug and gene delivery to tissue systems such as the cardiovascular system, the brain, cancerous tissues and skin. While these first threesystemsaretargetsforthedrugandgenetherapeutics,skinis usually not the target tissue; the objective is usually to get the therapeutic through the skin and into the circulatory system.

We trust that the compilation of review articles contained in this issue will endow the reader with information and insight, will enthuse the clinician with current and future technologies for non-invasive therapy, and will motivate the researcher with the perseverance required to attack the remaining obstacles and continue to push forward the frontiers of ultrasonic drug and gene delivery. Why should non-invasive healing be limited to magic wands in fairy tales? Such healing may soon become part of our lives through ultrasonic drug and gene delivery.

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