Pressure waves: A platform for drug delivery

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Pressure waves, photomechanical waves or laser-induced stress waves are terms that have been used to describe high amplitude pressure transients generated by lasers. They are unipolar compression waves characterized by a relatively fast rise time and a duration that ranges from a few hundred nanoseconds to a few microseconds. Pressure waves are, perhaps, one of the latest technology platforms for drug delivery. Pressure waves have been used to deliver macromolecules (including genes) through the cell plasma membrane both in vitro and in vivo, the nuclear envelope, the skin and they have been shown to enhance the permeability of microbial biofilms. The many diverse applications of pressure waves exemplify the potential of this technology for drug delivery in many different biological systems.

The applications of pressure waves for drug delivery rest on extensive studies of the interactions of laser-induced pressure waves with cells and tissue. In addition, shock waves generated by extracorporeal shock wave lithotripters and ultrasound have contributed to our understanding of the effects of waves on cells and tissue.

The interest in laser-induced stress waves goes back to the early seventies when short pulse lasers were introduced in medicine in order to reduce the collateral thermal damage of tissue. The concern, at the time, was that pressure waves could cause collateral mechanical damage to tissue. The first claim of tissue damage caused by pressure waves was made by Marshall in 1970. The early studies, however, could not always separate between the pressure-wave effects from other concomitant laser-induced effects. Furthermore, the magnitude as well as the characteristics of the waves were not known, so that no quantitative conclusions could be drawn. To investigate the biological effects of pressure waves in a systematic way, it was necessary to eliminate all other potential effects from the laser. The approach we took was to generate the pressure waves separately and launch them into cell cultures or tissue.

The idea that pressure waves could permeabilize the cell membrane came about from the observation that stress waves in the presence of a photosensitizer increased the cell killing. This was difficult to explain given that pressure waves do not produce any light. Interestingly, ultrasound and hematoporphyrin, a photosensitizer, also induced cell damage. Eventually, after all other hypotheses were proven wrong, it was shown that increased concentration of the photocensitizer in the cells caused increased dark toxicity. There were two other relevant observations. In the late eighties early nineties, it was shown that: 1) the combination of shock waves and chemotherapeutic drugs improved cancer treatment, although the mechanism of action was not known and 2) Shock waves, from extracorporeal lithotripters, were shown to permeabilize the cell membrane. So by the mid-nineties pressure waves were an established method for the permeabilization of the cell membrane. At about the same time it was shown that stress waves could also permeabilize the skin. Subsequent research investigated the effects of the pressure-wave parameters as well as the mechanisms of permeabilization. It remains to be seen whether pressure waves will move from the lab-bench to the bedside for the benefit of patients.