Development of novel shockwave-based needle-free vaccine delivery systems for human use

The most commonly used needle and syringe method for drug administration has come under scrutiny in the recent decades because of factors like needle contamination, requirement for safe disposal of used needles, waste accumulation, accidental needle-stick, pain during usage and needle phobia. Therefore, many new alternative non-invasive means of drug delivery have been developed, which mainly use oral, pulmonary, nasal, buccal or transdermal routes of administration. Among these, the drug transport through human skin proves to be more advantageous compared to the other routes due to the ease of administration, immuno-surveillance functions and easy accessibility. Liquid-jet injectors, powder immunization and microneedles are some of the budding technologies for transdermal delivery of drugs. Many methods to improve the efficiency of transdermal therapeutic systems by enhancing the driving force to increase the rate of drug transport have also been suggested. However, these techniques face major challenges due to the selectively permeable nature of the human skin and its ability to restrict molecular transport.

Shockwaves are non-linear waves, propagating at speeds greater than the speed of sound, with a unique characteristic of instantaneously increasing the pressure, temperature, and density of the medium through which they propagate. For over a half a century, the phenomena of shockwaves have been synonymous with aerospace research. The emerging paradigms of present-day shock wave research have opened new horizons for interdisciplinary applications. Shockwaves have been extensively used for various medical procedures like extracorporeal lithotripsy, treatment of avascular necrosis, accelerated bone fracture healing, angiogenesis, and tendinitis. The use of shockwaves as a driving force for transdermal drug delivery has proved to be effective because of their ability to accelerate the drug particles to high velocities so that they can penetrate the skin. However, the use of either compressed air bottles, ignition of detonable mixtures or operation of bulky and expensive instruments to generate shockwaves, make these techniques undesirable. Also, many of the techniques result in the accumulation of waste and production of harmful by-products during the detonation of mixtures.

Our group has been working on developing biomedical application so shockwaves using in-house developed devices. In the past, we have developed multiple shockwave-assisted vaccine delivery devices that can generate high velocity jets. BCG and *Salmonella* vaccine strains (DV-STM-07) have been successfully injected using this device in the mice model. The device has been optimized to obtain penetration depths of ~100 μm in the skin. Extensive studies in laboratory animals have been performed and have been published in peer-reviewed journals.

The proposed project deals with the further development of the device to make it useable in higher animals *(non-human primates*)* and eventually in humans *(* Subject to ethical clearance)*. PhD work will involve the following tasks.

1. The device must developed/optimized to achieve variable depths of vaccine deposition
2. The device must be developed for vaccines of different viscosities
3. Automation and systems integration to deliver a hassle-free device for clinical use