Implantable Pump Actuated by Static Magnetic Field for On-demand Pulsatile Drug Delivery

Seung Ho Lee1 and Young Bin Choy*1,2, 3

1Institute of Medical & Biological Engineering, Medical Research Center, Seoul National University, Seoul, 110-799, Republic of Korea 2Interdisciplinary Program in Bioengineering, College of Engineering, Seoul National University, Seoul, 152-742, Republic of Korea 3Department of Biomedical Engineering, Seoul National University College of Medicine, Seoul, 110-799, Republic of Korea

shlee0311@snu.ac.kr

Purpose: To achieve on-demand pulsatile drug delivery, we prepared an implantable pump actuated by static magnetic field (MDP). Thus, after implantation, the MDP could release the drug only at the time of actuation when a static magnetic field was applied form the outside of the body. By adjusting the number of outlets and actuations from MDP, we could vary the amount of delivered drug as well as maintain the plasma drug concentration in living rats for 30 days. Therefore, we conclude that the MDP is a promising implantable device for on-demand, pulsatile drug release.

Methods: To prepare an MDP, poly (methyl methacrylate) (PMMA) plates and pipes were cut and shaped, using a CO2 laser (FC-200RA Laser Machinery, Korea), to prepare the subunits, which were then assembled to prepare each of the units, i.e., a drug reservoir, cylindrical chamber and plunger. Three outlet holes, each 700 µm in diameter, were formed at the bottom of the chamber for drug infusion. The heads of the plunger and cylindrical chamber contained the magnets, facing each other with the opposite polarity to have them attached, thereby closing the outlet holes when not actuated. After that, the units were assembled again to prepare the MDP with the dimension, 20 mm in diameter and 13 mm in height (Figure A(a)). A single actuation was processed as described in the following: 1) a static magnetic field was applied on top of the MDP and the plunger moved up to suck the drug solution into the chamber (Figure A(b)), and 2) a static magnetic field was removed and the plunger moved downward to push the drug solution to the outside via the outlet holes (Figure A(c)).

Results: We carried out in vitro release test to investigate the performance of the MDP. One or three consecutive actuations were applied via a static magnetic field applied only at predetermined times and drug released in the media was detected right before and after actuations. As shown in Figure (B), drug was not released during the period between the times of actuations, indicating no leak from the MDP. Right after actuations, the amount of drug release was reproducible, which was 112.0 ± 2.46 µg and 338.6 ± 20.9 with one and three actuations, respectively. In this work, we also performed the pharmacokinetic study with the MDP, subcutaneously implanted in Sprague-Dawley (SD) rats for 30 days. The pump could be actuated noninvasively by applying the magnet on the skin right above the implanted MDP. When one and three consecutive actuations, the drug concentration in blood was measured to be 92 ng/ml ~ 146 ng/ml and 210 ng/ml ~ 363 ng/ml, respectively.

Figure (A) Schematic images of the MDP (B) In vitro drug release profile of MDP with one and three consecutive actuations at predetermined times (C) In vivo pharmacokinetic profile of the MDP implanted in SD rats.

Conclusion: In this work, we developed an implantable pump enabled with on-demand drug delivery. The pump herein (MDP) could be actuated by static magnetic field, thereby no need of an additional power source. Because of this, the pump could be actuated noninvasively after in vivo implantation. We demonstrated that drug delivery could be tuned simply by varying the number of actuations in the MDP, which was shown effectively operative in both in vitro and in vivo environments. Therefore, we conclude that the MDP is a promising implantable device for on-demand, pulsatile drug delivery.

Acknowledgments: This study was supported by a grant of the Korea Healthcare technology R&D Project, Ministry for Health, Welfare & Family Affairs, Republic of Korea. (HI14C2194).