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Automatic Intramyocardial Stem Cell Injection Device

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Treating heart failure by injecting mesenchymal stem cells (MSC) into the myocardium via an injection device and a needle-tipped catheter is a novel approach that can improve quality of life. The procedure is currently performed manually (10 - 14 sequential injections), so MSCs are delivered into the myocardium at an uncontrolled flow rate with susceptibility to rapid injections that reduce cell retention in the myocardium and induce cell reflux and damage. While slower injection rates improve cell retention, they incite operator hand fatigue, generating inconsistent cell delivery that causes therapeutically ineffective MSC clumping. As a result, a novel automatic injection device is required to improve stem cell delivery and enhance the clinical success of intramyocardial MSC injections. The design must integrate with the procedural syringe-catheter system, limit operator intervention to promote clinical use, provide controlled injection rates to maximize cell retention, maintain standard cell viability, and act as a research tool to inform and optimize treatment. It also needs a feedback system that displays the injection force throughout each procedure, increasing injection efficacy by assisting with catheter insertion and establishing catheter obstruction susceptibility. Although existing infusion pump systems and automatic injection devices are a promising solution, they are not approved for stem cell delivery, are not compatible with the intramyocardial syringe-catheter system, and can not display intramyocardial MSC injection forces in real-time. These are critical limitations that prevent their use, especially since MSC viability is pertinent to the success of each procedure.

To achieve accurate injections, the injector consists of a stepper motor that autonomously rotates a threaded rod to drive a force application block toward the procedural syringe, injecting 0.5 mL of MSCs into the myocardium at a 30 or 60 second injection rate. A syringe mold and clamp within the injector base fastens the required 1 mL syringe in place, preventing any displacement during each injection. Following each successful injection, the force application block moves back to the starting position, allowing syringe removal and insertion to take place within the required 60 second dwell time between injections. The injector feedback system is controlled by an Arduino Uno microcontroller and detects force via an FSG force sensor attached to the force application block, receiving and displaying the force applied by the injector to the syringe throughout each procedure. An LED built into the feedback circuit signals when the 4.10 N threshold is reached to indicate potential catheter obstruction. The entire system is battery operated and thus portable, displaying its clinical translatability.

Injection testing verified that each injection rate delivered the complete 0.5 mL of solution within the required time. FSG sensor reliability and force detection testing confirmed that all output force values over the typical injector force range were within the required 5% error margin, containing an accuracy of 0.93% with a standard error of 0.26%. Threshold testing identified 4.10 N as the catheter obstruction value and validated that the LED turned on when the FSG received this force. Following assembly of the entire injector, MSC viability testing verified that the 30 and 60 second injection rates maintained MSC viability within 5% of initial cell survival, in congruence with typical intramyocardial injections. Overall design functionality was confirmed with bovine skeletal muscle and *ex vivo* porcine heart injections that mimicked the clinical procedure. They demonstrated 0.5 mL of MSCs were properly delivered with both injection rates and that the FSG feedback system correctly displayed force values and alerted the user when threshold was exceeded. By performing these injections with a pressure sensor, intramyocardial injection force and pressure values were also established.

The extensive design specification testing results validate the efficacy of the injection device, confirming its reliability, accuracy, and clinically informative research capability. The injector provides the required 30 and 60 second injection rates that maintain cell viability and maximize cell retention. Its automatic MSC delivery at the required flow rates and dwell time limits operator intervention, meeting design specifications and promoting its clinical applicability. The feedback system accurately receives and displays the force throughout each injection, correctly alerting the operator when catheter obstruction is imminent. As a result, it meets all feedback system requirements, providing a simplistic interface that assists the operator with each injection, increasing MSC injection procedural success. With the injection device, the user is no longer subject to hand fatigue and the susceptibility to rapid injections is removed, promoting clinical efficacy. Through identification of the catheter obstruction force value and procedural force and pressure ranges, the injector is a research modality that is guiding and informing clinical injections, enhancing their effectiveness. This device is thus a critical component for improving the treatment of myocardial infarction and mitigating cardiac arrest risk.