Automatic Intramyocardial Stem Cell Injection Device

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TEAM: HEARTTHROB
PARKER ESSWEIN, MACY FRANK, LARS KRUGEL, VANESSA OBRYCKI, GAB ZUERN
ADVISOR: DR. MELISSA KINNEY   CLIENT: DR. AMISH RAVAL

Abstract

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 with 10 - 14 sequential injections of a 0.5 mL MSC aliquot solution over a 30 or 60 second duration. Unfortunately, manual injections result in an uncontrolled flow rate, inconsistent cell delivery, and operator fatigue. This can limit cell retention or induce cell reflux, damage, or clumping. An automatic injection device is thus required to improve stem cell delivery and enhance the clinical success of intramyocardial MSC injections. Existing automatic injection devices are insufficient since they can not display intramyocardial MSC injection forces and are not approved or tailored for this procedure. As a result, a novel automatic injection device was fabricated that integrates with the procedural syringe-catheter system, limits operator intervention, provides two controlled injection rates (30 and 60 seconds), maintains standard cell viability, constantly displays injection forces, and alerts the operator if catheter obstruction is imminent (illumination of a red LED when 2.40 N is exceeded). Validation testing was performed and the results confirmed that MSC viability did not decrease by more than 5% from the initial viability, the force feedback system was accurate and consistent, and the device delivered 0.5 mL of solution in 30 and 60 second intervals. This demonstrates that the device has the potential to enhance procedural success.

Problem Statement and Motivation

- Cardiovascular disease is the leading cause of death in the U.S., correlating to 696,962 deaths in 2020 [1]
- ~5 million people experience heart failure annually with over 250,000 deaths [2]
- Intramyocardial injections can help with cardiac repair but manually performing 10 - 14 injections can limit treatment
  - Uncontrolled flow rates
  - Operator hand fatigue
  - Rapid injections
  - Reduced cell retention
  - Cell reflux, damage, and clumping
- Current injection devices → Insufficient for this procedure

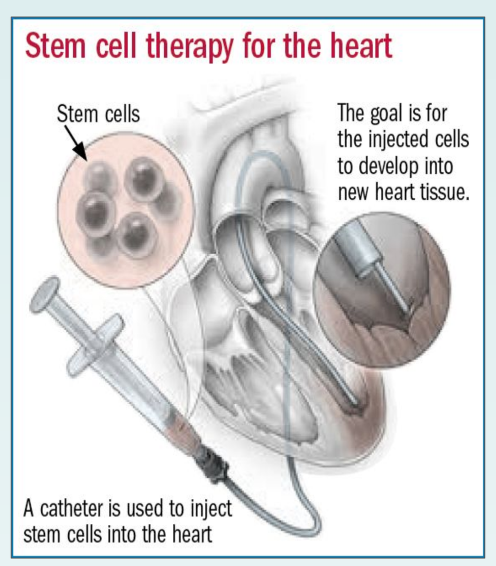

Figure 1: Stem cell therapy in the myocardium [3].

Background Research

- Current Cardiovascular Disease Treatment
  - 25 - 50% mortality rate within 5 years [4]
  - Limited success with current treatments (e.g., LVADs and medications)
- Mesenchymal stem cells (MSCs)
  - Derived from bone marrow [5]
  - Therapeutic potential [6]
- Flow rate
  - Too fast or too slow
    - Damaging to cells [7]
    - Off-target effects
    - Cell Clumping
  - Rate inconsistency

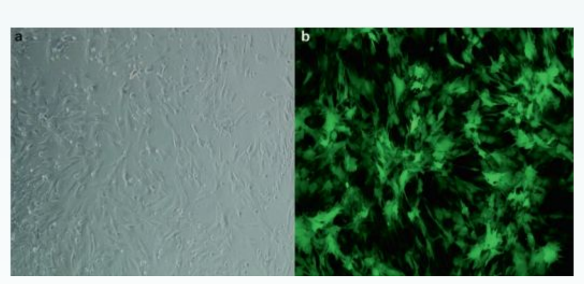

Figure 2: Mesenchymal stem cells in culture [8].

Design Criteria

- Electronically inject MSCs into the myocardium
  - Maintain cell viability - 5% reduction threshold
- Integrate with standard catheters, medical grade tubing, and 1 mL procedural syringes
- 30 and 60 second injection rates (± 1.00 second)
  - Deliver 0.5 mL of solution (5% error margin) [9]
- Force sensing resistor and visual feedback
  - Threshold = 2.40 N [10]
  - Applied force displayed throughout procedure
  - 20% error for force application less than 1.00 N
  - 15% error for force values greater than or equal to 1.00 N
- Budget of $3000 and manufacture cost of $500 [11]

Final Prototype

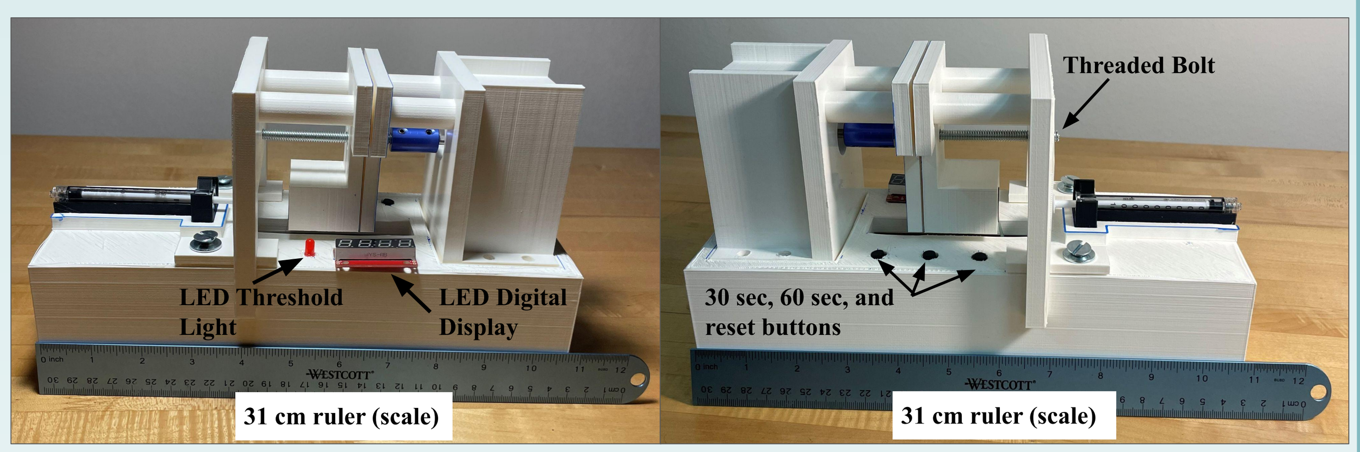

Figure 3: Right and Left end view of the injector prototype displaying the threaded bolt force system, injection buttons, and feedback system.

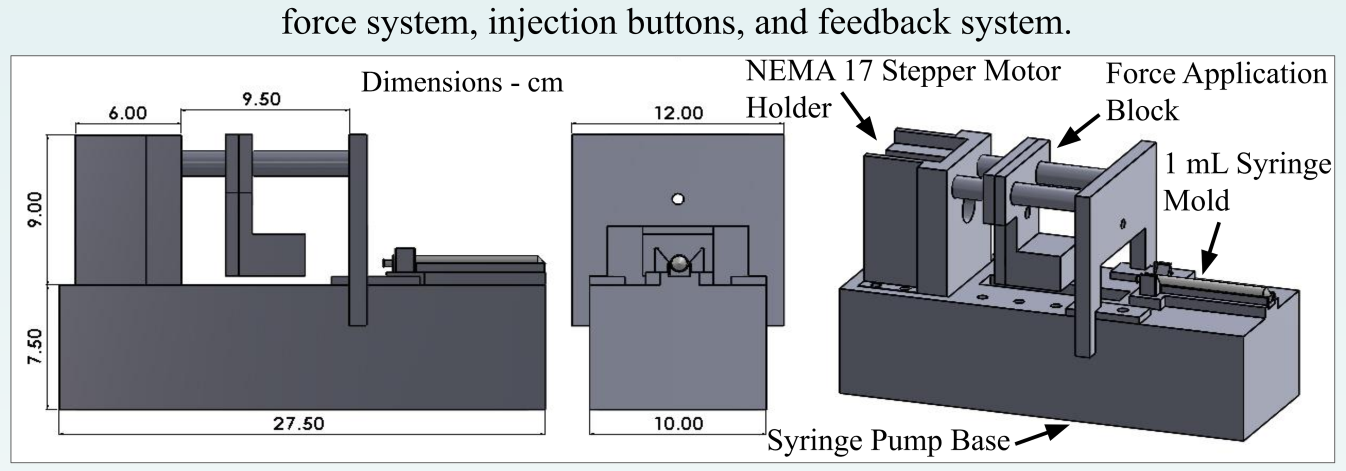

Figure 4: Solidworks drawing of final prototype assembly.

- Prototype features
  - 30 second and 60 second controlled injection rates
    - Start, pause, reset, and adjust functions
    - Regulated via NEMA-17 Stepper Motor (Figure 5)
  - Applied force feedback system
    - Detects force via an FSR 400 series force sensor
    - Controlled by Arduino Microcontroller and calibration curve
    - LED threshold light warning and digital display
  - 1 mL syringe mold

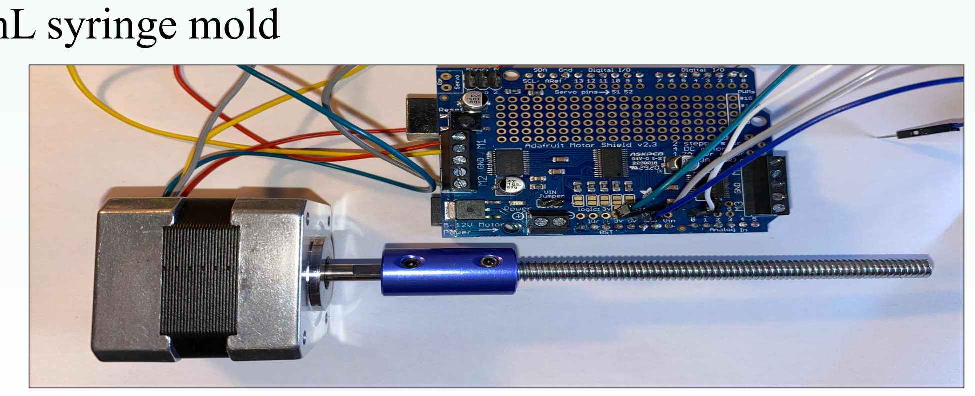

Figure 5: Arduino Motor Shield, NEMA-17 Stepper Motor, and 5 mm to 0.635 cm coupler.

Testing and Results

- Feedback System Reliability Testing (n = 3) - Calibration Curve

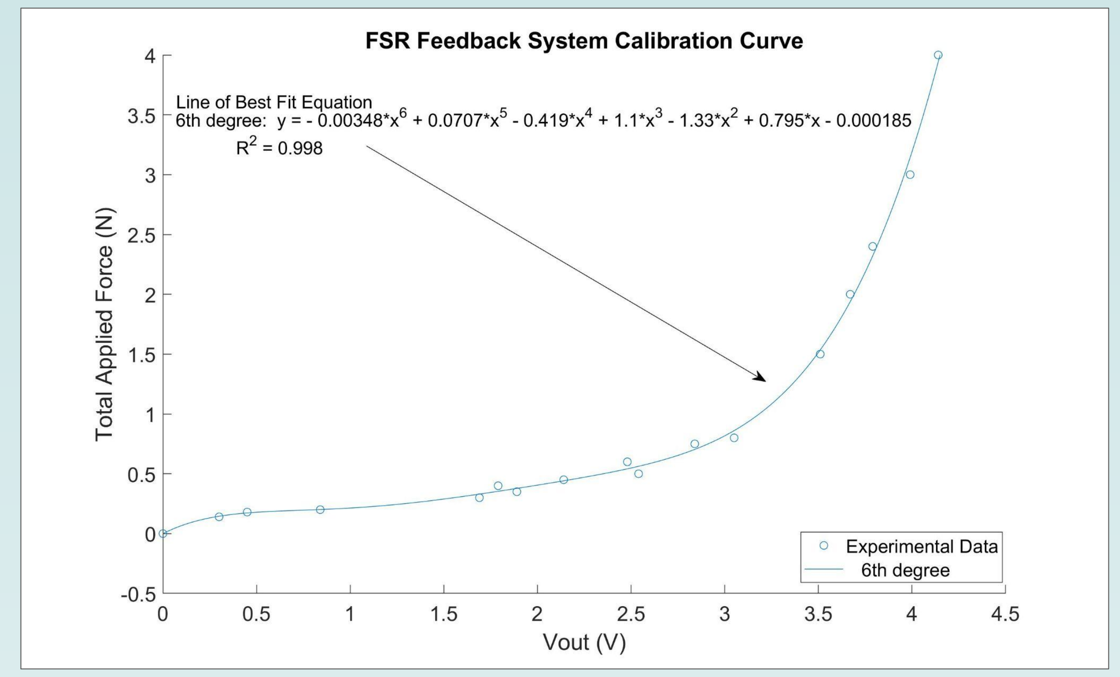

Figure 6: Calibration curve for the FSR feedback system under various loading enabling applied force calculation.

- Feedback System Testing
  - Force Detection Testing
    - Less than 1.00 N - Average error = 15.78 ± 1.33%
    - 1.00 N and above - Average error of 7.18 ± 4.50%
  - LED Threshold Testing - **Passed**
  - LED Digital Display Accuracy Testing - 0.14 ± 0.15% discrepancy between scoreboard and serial monitor
- Syringe Mold Testing (n = 5) - **Passed**
- Stepper Motor Rate and Distance Testing (n = 5) - **Passed**
- Cell Viability Testing (n = 5) - ANOVA p-value = 0.41

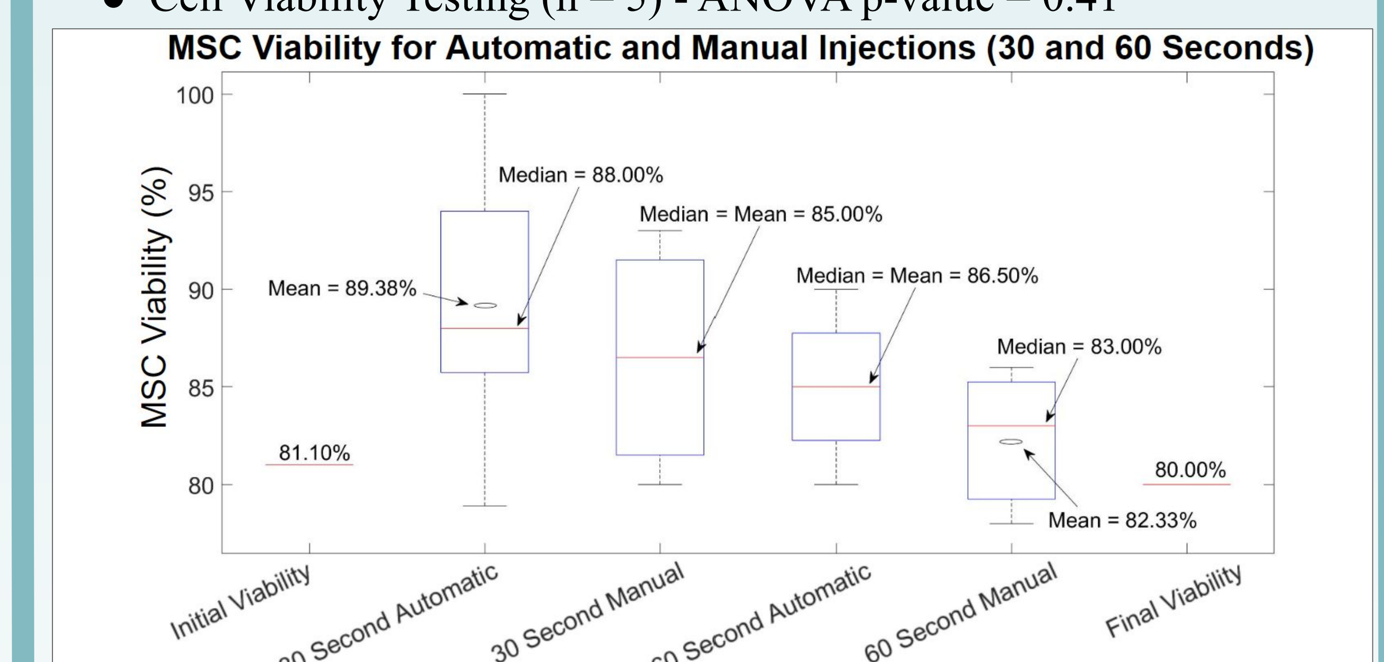

Figure 7: Boxplot comparing the viability of MSCs following automatic and manual 30 and 60 second injections.

- Fully Assembled Injector Testing (n = 5)
  - Volume and Rate Testing (Table 1)
  - Clinical Procedure Simulation
    - 30 and 60 second injections (± 1.00 second)
    - Delivered ~0.5 mL of solution from 1 mL syringe

Table 1: Average injection rate durations and delivery volumes including percent error.

Injection Type	Average Injection Time (seconds)	Average Injection Volume (mL)	Percent Error Between Injection Time and Target Time (%)	Percent Error Between Injection Volume and 0.5 mL (%)
30 Second Injection	30.57 ± 0.12	0.49 ± 0.01	1.88 ± 0.41	3.60 ± 1.67
60 Second Injection	60.19 ± 0.15	0.48	0.26 ± 0.25	4.0

Conclusion and Discussion

- Efficacy of the injection device validated
- Provides required 30 and 60 second injection rates
  - Maintains cell viability and promotes cell retention
- The feedback system accurately receives and displays the force throughout each injection
  - Alerts the operator when catheter obstruction is imminent
- Reliable and Accurate - Clinical applicability
- Automatic MSC delivery limits operator intervention
  - Eliminates operator hand fatigue and rapid injections
- Implication: Improve intramyocardial MSC injections, enhancing myocardial infarction treatment

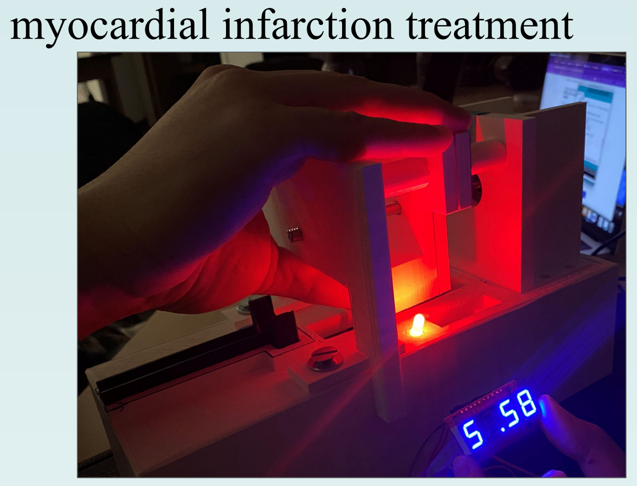

Figure 8: Illuminated threshold LED and digital display.

Future Work

- Extensive feedback system testing in different situations
  - Test accuracy against various viscosities
- Perform bovine steak and *ex vivo* heart injection testing
- Establish force ranges associated with different myocardium locations
  - Diseased/scarred tissue, healthy tissue, and body cavity
- Complete *ex vivo* catheter obstruction testing
- Incorporate a cell agitation apparatus
- Transition the injector into battery operation

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