Development of Myocardial Slices for Cardiovascular Studies

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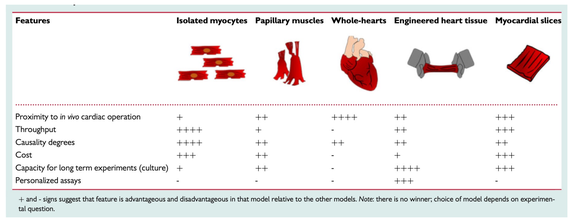
Abstract

Heart disease and failure remain the top causes of death in the world, even with the many new advancements in the field. Gaining a deeper understanding of the heart can prove to be beneficial for saving lives. Myocardial slices, which are cut to 1-centimeter square and 100 to 400 µ thin, are slices of living muscle tissue from the heart. For testing, the slices are cut from animal hearts. The myocardial strips are then examined, looking at the contractile function of the heart as the living slices contract and expand. A literature review identified the best-suited platform to induce mechanical stimulation onto myocardial sheets. This system is anticipated to support multi-sensory analysis of myocardial tissue response to stretch. Improvements in analyzing myocardial strips can help future heart research to minimize heart-related problems.

Introduction



Features	Isolated myocytes	Papillary muscles	Whole-hearts	Engineered heart tissue	Myocardial slices
Proximity to *in vivo* cardiac operation	+	++	++++	++	+++
Throughput	++++	+	-	++	+++
Causality degrees	++++	++	++	++	++
Cost	+++	++	-	+	+++
Capacity for long term experiments (culture)	+	++	-	++++	+++
Personalized assays	-	-	-	+++	-

+ and - signs suggest that feature is advantageous and disadvantageous in that model relative to the other models. Note: there is no winner; choice of model depends on experimental question.

Figure 1: Different cardiac models

- There are a multitude cardiac models.
- Each model has their own pros and cons.
- This research involves using myocardial slices.
- The model chosen depends on the goals and procedure for the study.
- Majority of heart slices comes from animals, not humans.
- The animal heart slices are closely comparable to those of a human.

Methodology

- Myocardial slices are cut from a small mammal's heart, such as rats and rabbits, with a high precision microtome.

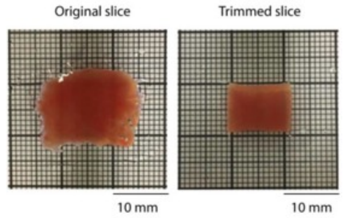


Figure 2: Myocardial slice before and after being trimmed.

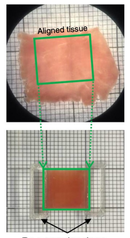


Figure 3: Myocardial slice is glued in the 3D printed rings.

- The myocardial slices are then placed and glued in a specifically designed 3D printed ring to allow for the mounting on the designed metal stretcher.
- The rings with the myocardial slices are then places on the designed metal stretcher.

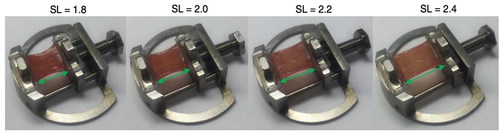


Figure 4: The myocardial slice is placed on the slots that hold the 3D printed rings.

- The mounted and stretched myocardial slices are placed in a culture chamber for 24 hours. The culture chamber electrically stimulates and oxygenates the slices.
- Unmounted myocardial strips are placed in a six-well plate with liquid media for 24 hours. This is the control group.

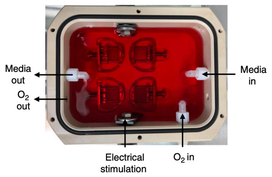


Figure 5: Metal stretchers are placed in the culture chamber.

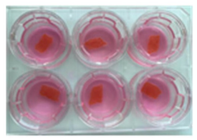


Figure 6: Unmounted myocardial slices are put in the six-well plate.

- Contractility, gene expression, and rate of decay are analyzed. The loaded and unloaded (control) groups are compared after analysis.
- There were four conditions: 0 hours, unloaded, sarcomere lengths (SL) = 1.8 µm, SL = 2.0 µm, SL = 2.2 µm, and SL = 2.4 µm.

Results

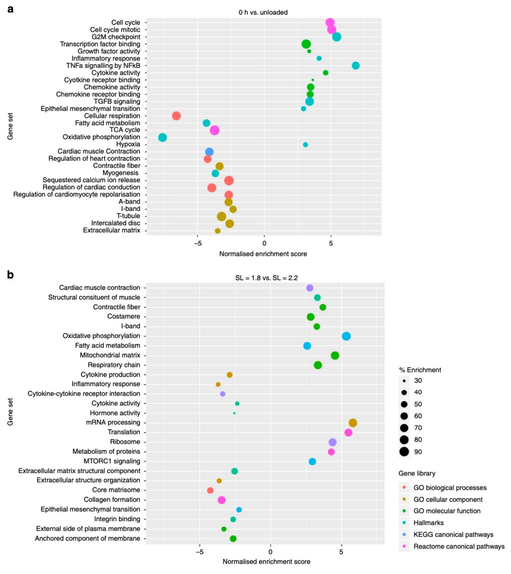


Figure 7: Gene expression of the myocardial slice after being cultured for 24 hours.

- A positive normalized enrichment score on the graph means that there is an enrichment of that gene set, seen on the y-axis.
- The SL = 2.2 µm condition's gene sets had the most energy production and cardiac muscle contraction.
- Genes related to negative tissue effects, such as inflammation, were lower for the SL = 2.2 µm condition.
- Genes related to protein synthesis and the breakdown of protein were found to be more activated in the SL = 2.2 µm condition.

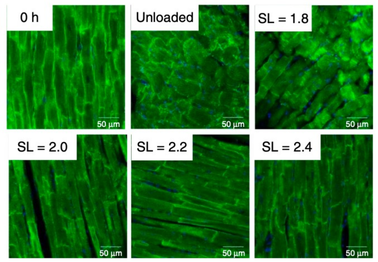


Figure 8: The myocardial slices after being cultures for 24 hours

- The area of the average cardiomyocyte was more preserved at SL ≤ 2.2 µm.

Discussion/Conclusion

- The mounted and stretched myocardial slice at SL = 2.2 µm with electromechanically stimulation is more preserved over time when compared to the unmounted control and the less stretch slices.
- Using animal myocardial slices has been proven to be effective in heart research and can translate to the human heart.
- There has been a significant amount of development of myocardial slice research over the past years.
- There are still advancements to be made with devices to aid the testing of myocardial strips.

Acknowledgements

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