Design, fabrication, and evaluation of an accessible moving pillar system for in vitro skeletal muscle tissue pacing

By N.E.M. Klein Hofmeijer[1], C. Rivares Benitez[1], J. Rouwkema[2], M. Sartori[1]

[1] Neuromuscular robotics University of Twente, The Netherlands; [2] Engineering Organ Support Technologies University of Twente, The Netherlands

SCAN ME

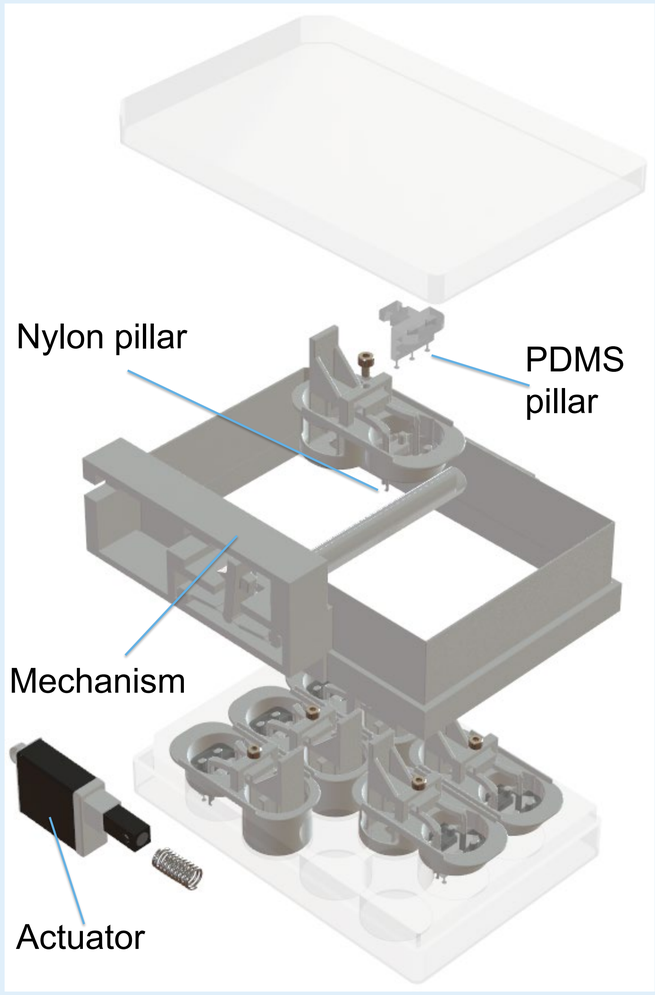


Introduction

Understanding **skeletal muscle** structural **remodelling** is key for developing **personalized physical training** and **rehabilitation interventions**. However, accessing remodelling in human muscles is challenging and often **invasive**. An ***in vitro*** platform capable of applying **mechanical and electrical stimulation** to tissue engineered skeletal muscle (TESMs) can therefore be highly valuable. Collected data can potentially be used for **modeling** and **controlling** the remodeling process. Moreover, no existing systems allow these effects to be studied across larger numbers of small engineered tissues across large temporal scales. While several platforms can engineer such tissues[1-3], they do not incorporate **mechanical stimulation.**

Goal: **Designing and manufacturing a platform to mechanically and electrically stimulate engineered muscle tissues**

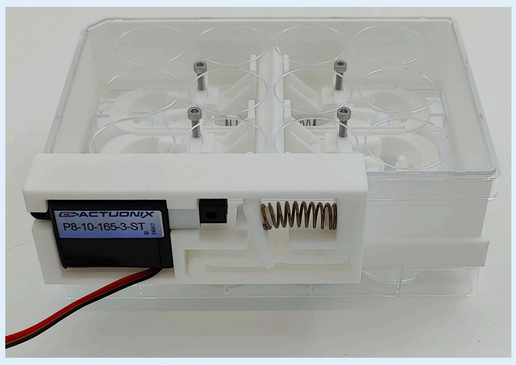
Design



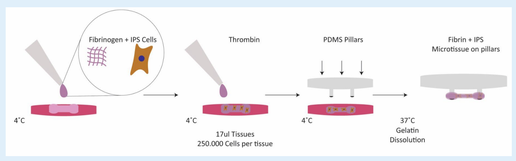
3D rendering of design

Based on a previously designed system by Ribeiro et al.(2022)[3], we **designed** and **manufactured** a **modular** device that applies mechanical stimulation to **3D-TESMs** by adjusting the distance between a bendable polydimethylsiloxane (PDMS) pillar and a movable Polyamide 2200 (Nylon) pillar which act as attachment points. **Six wells** are used, each with **two** mechanically stimulable and **one** control tissue. The **twelve** movable pillars are driven by **one actuator** using a mechanism. The current design allows for a **twenty-five** percent in/decrease in length.

Prototype



Prototype image

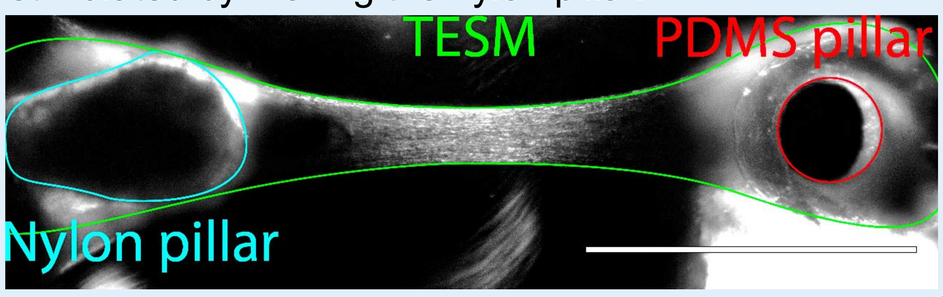


The tissue formation process

The design was converted into a working prototype. The mechanism and the nylon pillar were **3D printed** and a micro-stepper actuator was used to drive it. This resulted in a **low-cost**, **user-friendly** design.

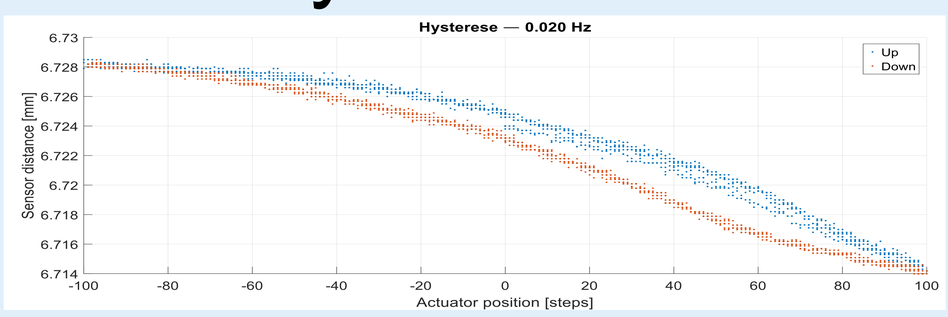
The setup is compatible with standard **inverted microscopes**, enabling real-time imaging and estimation of both **passive and active forces** from pillar **deflection**.

Human induces pluripotent stem cells are used to create TESMs by formation in gelatine moulds according to a combination of protocols[2-3]. The TESM forms around the pillars, as shown below and can subsequently be mechanically stimulated by moving the nylon pillar.

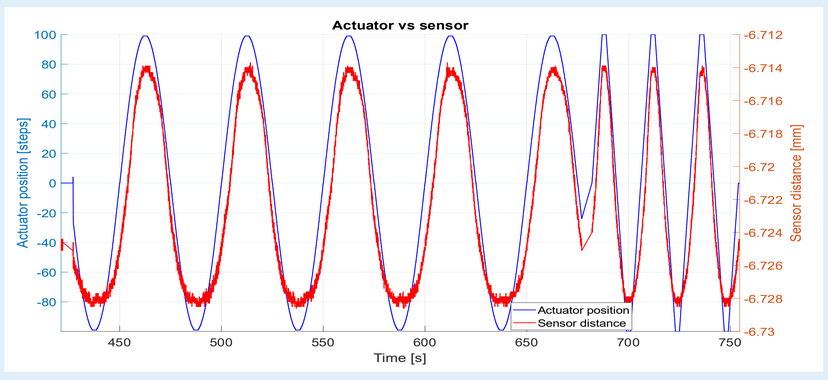


TESM on a deflectable PDMS pillar, and a stiff movable nylon pillar. Scalebar =1.8 mm

Mechanical preliminary results



Hysteresis plot of one of the six locations at 0.02 Hz trapezoidal movement.

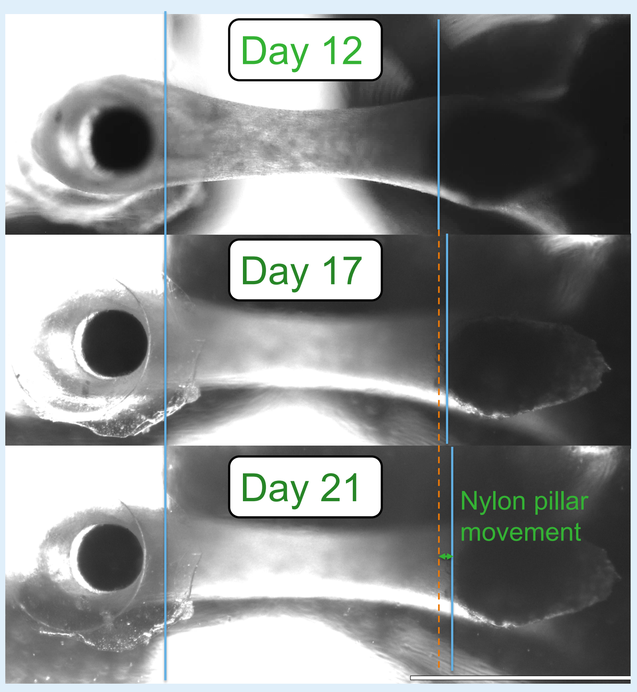


Time plot a 0.02 Hz sinus and trapezoidal movement.

Mechanical tests are conducted to analyze hysteresis, accuracy and repeatability. Above results are shown for one of the six wells. Location influences results, so further analysis is planned to show a clearer picture.

Biological preliminary results

A **21 day** biological experiment was conducted in which tissues were lengthened **twice** to promote **length growth**. Below Images of one of the tissue on three different days. Results are currently being evaluated and are expected soon.



Picture of tissue on three different days scalebar = 1.8 mm.

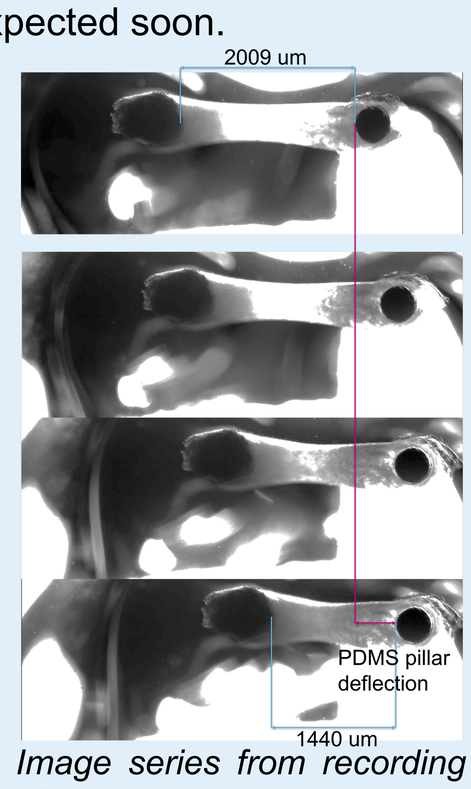


Image series from recording of nylon pillar moving with a tissue on the pillars.

In **conclusion**, the platform supports **3D-TESMs formation**, controlled **mechanical stimulation**, as well as **force quantification**, offering a potential system for advancing engineered muscle research.

Acknowledgements

Design based on platform developed by AST (university of Twente) Ribeiro MC et al.(2022). *J. Pers. Med.*, 12(2), 214.
Cells used for biological testing provide by Professor W.W.M. Pijnappel, Erasmus MC, Rotterdam, The Netherlands

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References

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[3]Ribeiro MC et al.(2022). *J. Pers. Med.*, **12**(2), 214.

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