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Wake Forest Institute for Regenerative Medicine

Multi-functional Solid 3D Organ Bioreactor Platform for Regenerative Medicine Applications

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Introduction

Cell-based tissue-engineered products require the use of tissue-specific bioreactor for preconditioning and maturation. However, clinically applicable tissue or organ-specific bioreactors are not available.

Objective

This study aimed to develop a solid organ bioreactor module containing a rotatable and pressurizable organ enclosure for integration into a standardized, self-contained, and multiplatform bioreactor that could precondition and mature solid organ construct.

Methods

Step 1: Determine bioreactor design condition

- Pump selection
- PID (proportional-integral-derivative) controller design
- Biomedical compatible material
- Pressure/flowrate sensor selection
- Tubing & connector selection

Step 2: Fabricate & assembly of bioreactor

- CAD design of all elements
- Modify the kidney 3D scanned file to generate CAD design of the inflatable kidney sac & solid organ enclosure
- Fabrication using 3D printer
- Assembly of all bioreactor parts

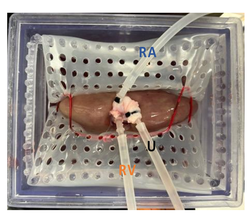
Step 3: Validate bioreactor design with biological scaffold

- Using porcine kidney for validation
- PID controller testing
- Long-term perfusion

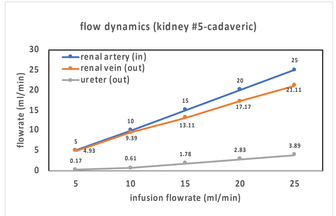
Results

❑ **Decellularization of porcine kidney for usage in system validation**

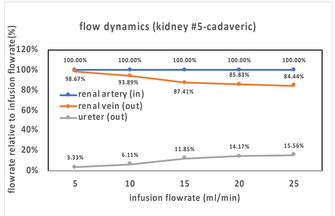
1A

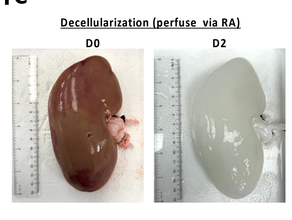


1B



1C



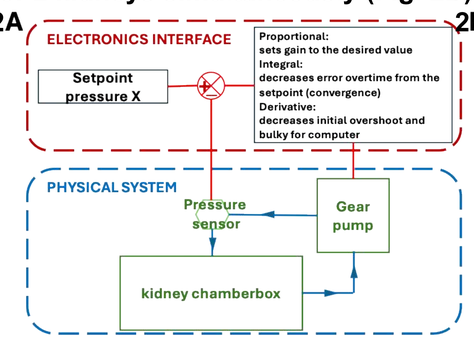


The fresh porcine kidney has been stabilized with silicone sac in upright orientation (Fig. 1A). The intactness of kidney has been validated with its flowdynamics monitoring (Fig. 1B). The kidney can achieve full decellularization within 2 days (Fig. 1C)

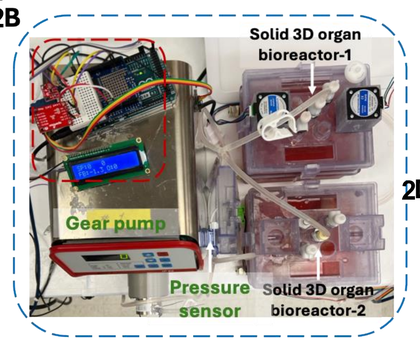
❑ **Benchtop test of PID controller using decellularized kidney**

The constant-pressure motion was carried out by integrating the flow pump, flow rate sensor, pressure sensor, and PID controller to minimize the delay or overshoot of the inflow pressure, which could lead to organ damage (Fig. 2A & 2B). The PID controller can generate stepwise pressure profile to condition porcine kidney (Fig. 2C) and the full setup can be used to perfuse 1 or 2 kidneys simultaneously (Fig. 2D).

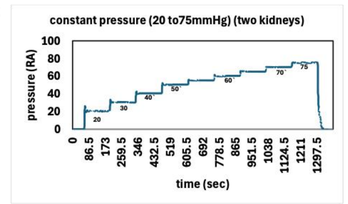
2A



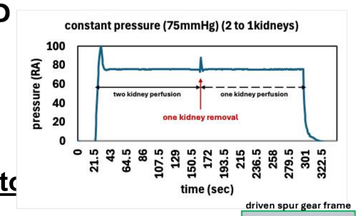
2B



2C

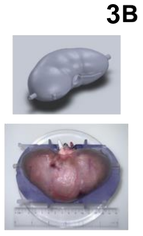


2D

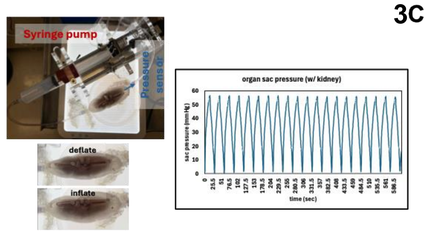


❑ **Rotatable & pressuresiable organ enclosure design & integration into**

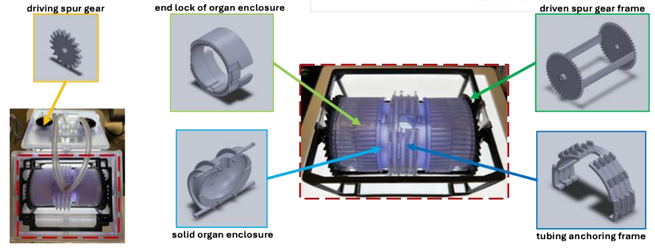
3A



3B



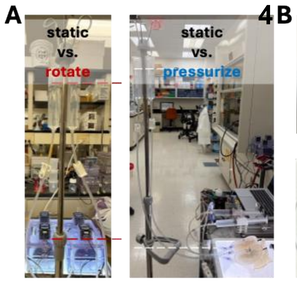
3C



The elastic kidney sac has been successfully 3D-printed (Fig. 3A). The syringe pump can externally apply pulsatile pressure to the kidney via the organ sac (Fig. 3B). The rotatable organ enclosure (Fig. 3C) can control orientation and minimize stress concentration during perfusion.

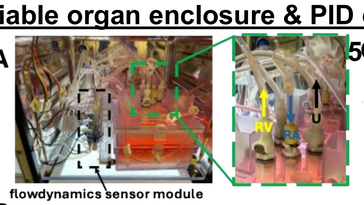
❑ **Validation of the rotatable & pressuresiable organ enclosure & PID controller on ex-vivo study**

4A

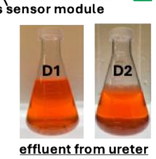


4B

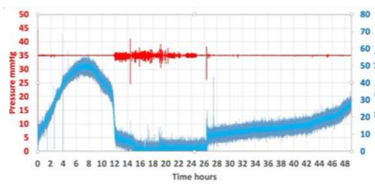
5A



5B



5C



The blue dextran dye has been used to validate the effectiveness of the rotary and pressurizable organ sacs in achieving even dye distribution (Fig. 4A & 4B). The PID controller has demonstrated its effectiveness in maintaining ex vivo porcine kidney viability with urine effluent (Fig. 5A, B & C).

Conclusions

This study successfully demonstrates the development and validation of a solid-organ module with a monitoring system, establishing a standardized modular bioreactor platform with potential applications across multiple tissue and organ systems.