# Evaluation of A Novel Organ Perfusion Research Platform

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***Abstract*— This paper presents a novel, low cost, organ perfusion machine designed for use in research. The modular and versatile nature of the system allows for additional sensing equipment to be added or adapted for specific research applications. Here we introduce the system and present its preliminary evaluation by assessing its ability to maintain a predetermined input pressure. A proportional-integral-derivative (PID) controller was implemented and tested on a porcine liver to maintain input pressure to the hepatic artery and compared to bench tests. The results confirmed the effectiveness of the controller for maintaining input through the hepatic artery (HA) in a timely manner.**

***Clinical Relevance*—Machine Perfusion (MP) is proving to be an invaluable adjunct in clinical practice. With its ongoing success in the transplant arena, we propose MP for wider use in basic and applied research. A cost-effective, versatile system that can be modified for specific research use to test new pharmacological therapies, imaging techniques or develop simulation training would be beneficial.**

## I. Introduction

Recent work has demonstrated the potential of machine perfusion to extend the period during which organs remain viable *ex vivo* from hours to days [1-4]. Although primarily being evaluated for the improvement of organ preservation, the ability to preserve whole organs in physiological conditions provides a testbed for answering basic scientific questions on the mechanism of a range of treatments from pharmacological interventions for chronic disease or cancer, to loco-regional therapeutic interventions. Additionally, a perfused whole organ can be used in the development of surgical training and simulation, making this platform a versatile option for the academic community. Following on from the success of the OrganOx Metra in the clinical arena [4, 5] the academic community may benefit from a similar form of perfusion machine designed specifically for use in a research setting. Such a machine would be designed to be modular in function allowing researchers to integrate specific functions as per their requirement and need.

A novel perfusion circuitry has been developed to produce a system to evaluate organs in a controlled, adaptable chamber. Real-time monitoring of several physiological parameters such as flow rate, pressure, oxygenation, and pH is in-built in the circuitry and can be adjusted as required. By utilising cleanable, reusable components, this system provides an affordable alternative to commercially available, clinical perfusion machines, with a total parts cost of approximately £11,000, including disposable parts cost of approximately £500. This paper presents preliminary findings on the system performance in bench experiments as well as when applied to the perfusion of a porcine liver.

## II. Materials and Methods

### A. System Design

The organ perfusion machine is designed to be inexpensive, robust, modular, and adaptable to various experimental purposes. A single centrifugal pump (PuraLev 1200 MU, Levitronix GmbH, 8005 Zurich, Switzerland) was used to circulate the perfusate through all elements of the system flow circuit. Pressure (Single Use Pressure Sensors, PendoTECH, Princeton NJ 08540, USA) and flow (SONOFLOW co.55/100, SONOTEC, 06112 Halle, Germany) sensors were used to monitor both the input and the output pressure and flow rates of the perfusate while a single oxygen (EOM-(t)-FOM, PreSens Precision Sensing GmbH, 93053 Regensburg, Germany), and temperature (Pt100, PreSens Precision

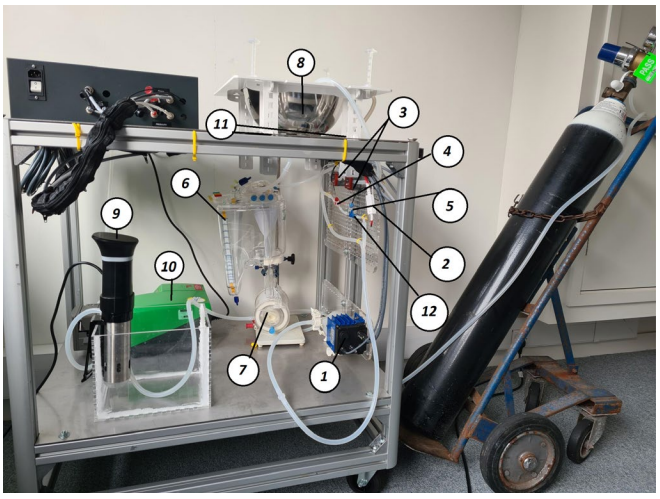


*Figure 1: An overview of a research-orientated perfusion system. (1) centrifugal pump, (2) pressure sensor, (3) flow sensors, (4) temperature Sensor, (5) oxygen Sensor , (6) reservoir (7), oxygenator (8), organ chamber (9), heat exchanger, (10) peristaltic pump, (11) load cells, (12) pH sensor.*

Sensing GmbH, 93053 Regensburg, Germany) sensor was used to monitor the input stream only. The organ was suspended via perforated plastic film over the organ chamber. Any runoff perfusate from the liver was collected and, along with the liver output flow, was returned to the 4 L reservoir, where it was filtered. The oxygenator, re-oxygenated blood from the reservoir before it was pumped back through the system. Four load cells, placed directly beneath the four supports of the organ chamber in a square formation, monitored the weight of the liver throughout the perfusion. Fig. 1 gives an overview of the system. Fig. 2 shows the circuit diagram of the organ perfusion system and how each sensor of the system integrates with the Raspberry Pi.

All peripherals were controlled via a single-board computer (Raspberry Pi 4, Raspberry Pi Foundation, Cambridge CB2 1NF, UK), and were communicated with using a combination of MODBUS (pumps, flow and pressure sensors), RS-232 (oxygen sensor), and RS-485 (pH sensors) communication protocols. An analog to digital converter (Waveshare 32-bit AD/DA board, Waveshare Electronics, Shenzhen, China) was used to interface between the Raspberry Pi and the pressure sensors. The software architecture was implemented using ROS2 to ensure modularity of system components. All sensor data was displayed in real time via a laptop interface and the output recorded for further analysis.

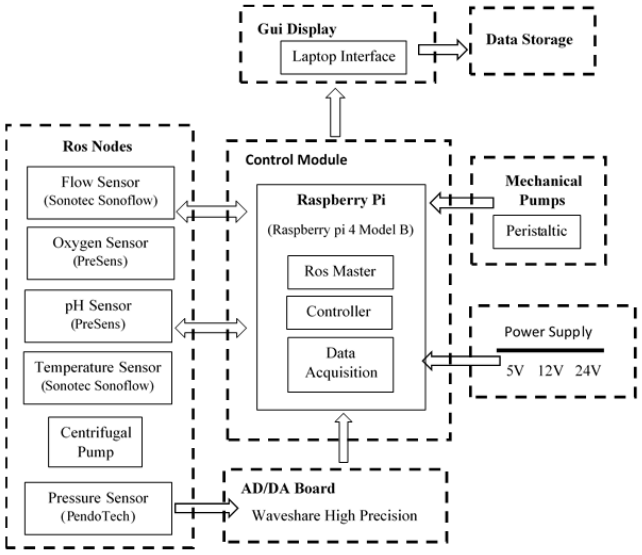


*Figure 2: Circuit Diagram of Organ Perfusion System.*

The system is designed to enable fine control of all peripherals but was primarily used in this study to control and maintain pressure through either of the two input vessels, the portal vein (PV) and hepatic artery (HA). Pressure could be controlled by directly adjusting the duty cycle of the centrifugal pump or using a closed-loop proportional-integral-derivative (PID) controller. PID is a commonly used feedback controller to regulate process variables such as pressure or flowrate. A desired set point is reached and maintained by adjusting an actuator to minimise the difference between the desired value and the current state. The gain parameters of the PID controller were tuned using the Ziegler-Nichols tuning method and the following

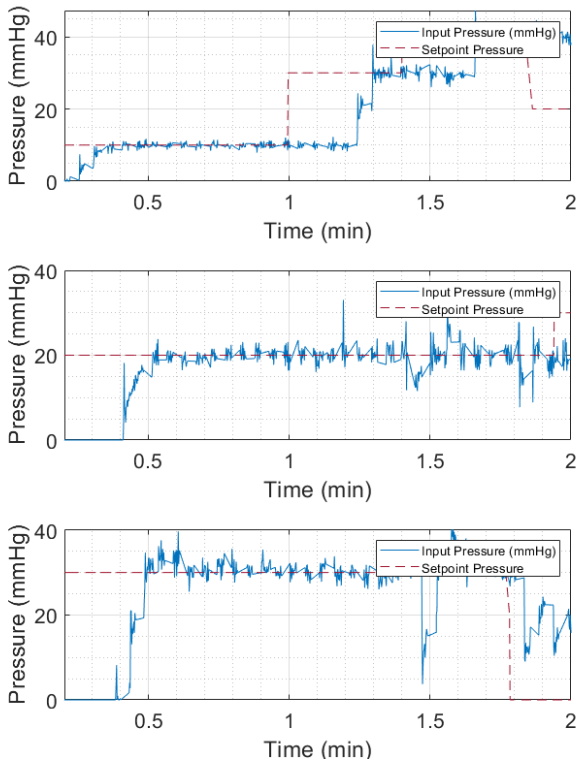


*Figure 3: Comparison of three pressure controller bench tests conducted on the perfusion system. A set pressure was established (red line). The response for each test was observed.*

parameters were obtained: $K_p = 5$, $K_i = 2$, and $K_d = -0.5$. These parameters were chosen based on achieving the shortest settling time while minimising potential overshoots.

### *B. System Test*

To evaluate suitability of the system for organ perfusion, the PID controller was initially tested without a load to observe the response prior to a test with a porcine liver. The system was set to monitor the two input and output pressures in the system as well as the centrifugal pump speed. The target pressures were set to values between 0 mmHg and 40 mmHg in all conditions, the results of which are shown in Fig.3. Step responses from these tests indicates a settling time of approximately 12 s and a rise time of approximately 6 s. Additionally, the tests indicate a maximum overshoot of 10 mmHg.

### *C. Liver Procurement, Storage and Experimental Setup*

The liver was obtained from a domestic pig immediately following termination from a commercial abattoir. The bile duct was ligated to prevent bile leakage and the blood flushed from the organ using cooled heparinised saline solution. The PV from the pig could not be cannulated; hence, the PV input from the system was suppressed via pinch valves forcing the blood to flow through the HA input only.

The system was primed with 3 L of autologous whole blood retrieved from the pig after cardiac death. Additionally, 20,000 IU of heparin was added to prevent the formation of clots. After approximately two to three hours of cold ischemic storage, the liver was placed into the organ chamber of our system and connected via the HA and hepatic vein (HV). The

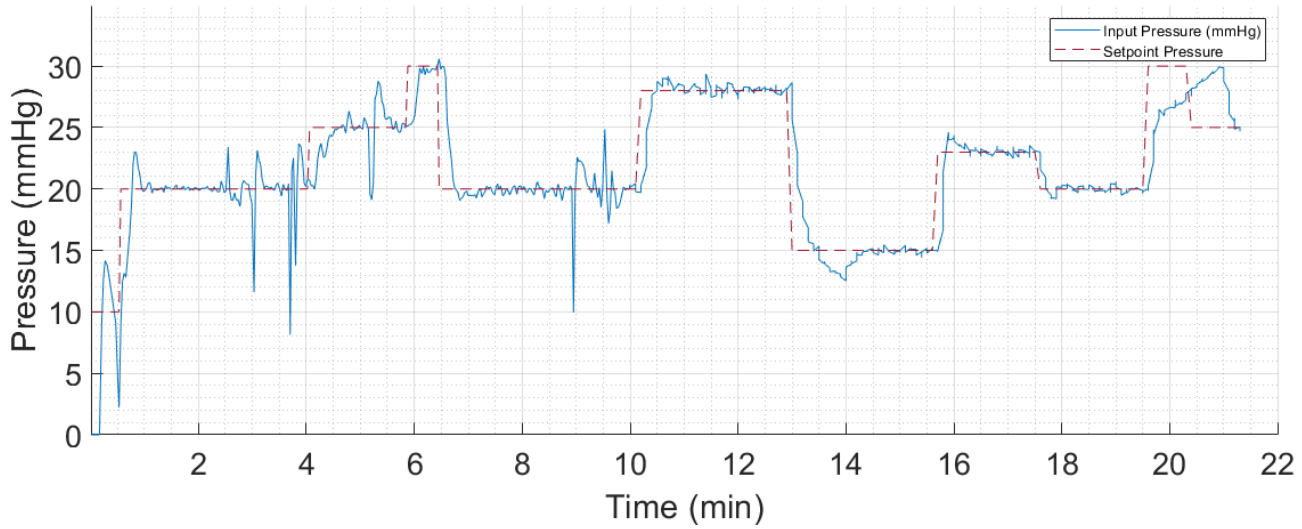


*Figure 4: Pressure sensor output while under the pressure controller. Red line indicates the desired input pressure while the blue indicates the input pressure reading.*

perfusate was warmed using a heat exchanger to a temperature of 29 °C. Machine perfusion was maintained for approximately 1 hour and initially controlled directly using the centrifugal pump.

Once outflow was established the system settled on and maintained the desired input pressure between 20 mmHg and 25 mmHg. Following this, further system tests were conducted while the liver was being perfused. Various HA pressure set points were established and maintained for several minutes while assessing the overall effect on the liver via the other sensing parameters, such as flow and O2 concentration. An input pressure limit of 30 mmHg and pump limit of 3000 rpm was established to prevent the deterioration of capillaries in the liver.

## III. Results

The system was set to perfuse the liver for approximately 20 minutes. Throughout the experiment, step signals of 15 mmHg – 30 mmHg were used to test the system's adaptability. In the first 10 minutes disturbances were added to the signal by introducing external pressure changes to the system. These disturbances were a combination of short one-second or five-second pulses implemented before and after each pressure sensor in the system. These parameters were chosen to minimise rapid fluctuations of the centrifugal pump as it tries to compensate for the change in pressure. Large fluctuations have the potential of stalling or damaging the pump. The results show sudden changes in pressure caused by these disturbances but no overall effect on the behavior of the controller. The pressure readings for blood flow into the liver via the HA are shown in Fig. 4 and indicate that the controller achieved a settling time of approximately 20 s and a small overshoot (less than 2 mmHg). Steady state appears to be achieved within 6 s – 10 s and remaining stable over time. A larger overshoot occurs with sudden decreases in pressure but remains relatively small and the control system

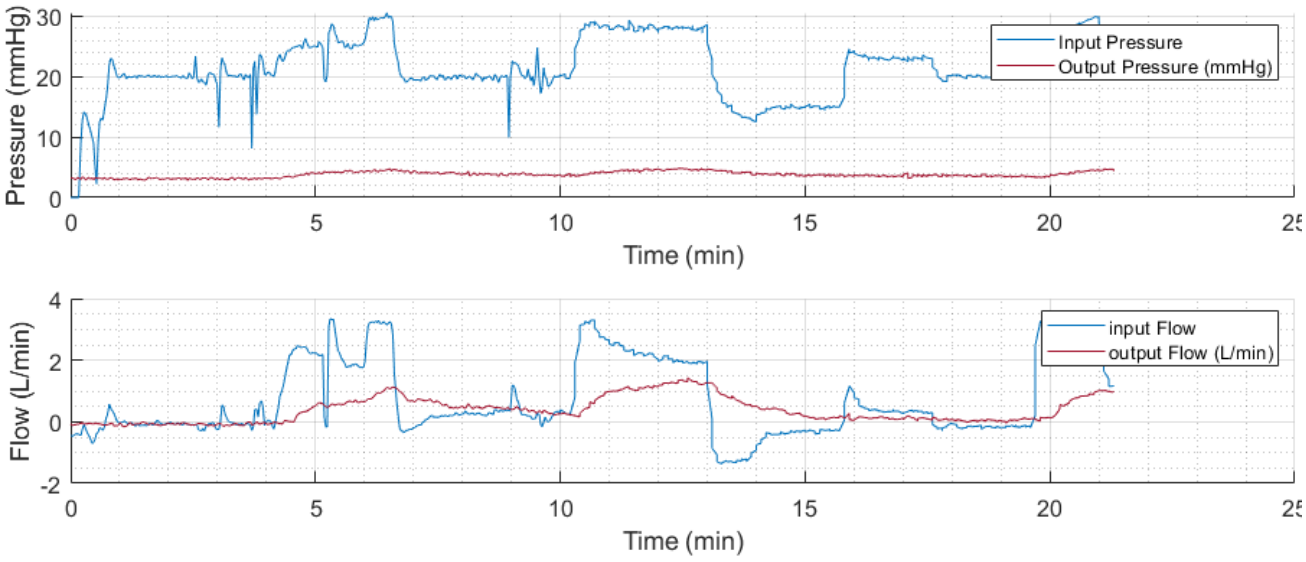


*Figure 5: Comparison of the input and output pressure (top) and flow (bottom) from the porcine liver. The effect of the pressure controller can be clearly seen in the input pressure and flow sensors.*

was able to follow the target pressure. The maximum attainable pressure reading was 28 mmHg – 30 mmHg due to the rpm limit of the centrifugal pump.

The behavior of the HA and HV flow rates are also shown in Fig. 5 and has been clearly affected by the controller. The input flow stabilises after a period and occasionally produces back flow at sudden pressure drops when the pressure target point is set more than 15 mmHg below the previous state, as indicated by the negative flow rates in Fig. 5. The output flow produces less drastic changes but can still be seen to follow the behavior of the pressure controller.

## IV. Discussion and Conclusion

In this study, we presented a novel computer assisted perfusion machine that has the versatility and adaptability to benefit the wider research community. The proposed system has the capability of dynamic monitoring of multiple parameters as well as fine-tuned control of pressure and flow. The underlying software that drives the system allows for further sensors to be easily implemented and customised towards the needs of the user. The efficacy of the system was tested in this study by assessing its ability to maintain a stable input pressure through the HA of a porcine liver.

Though unusual to receive a porcine liver without a portal vein, this did not pose a problem for the perfusion as the adaptability of the system allowed to overcome the challenges posed by this anatomical anomaly. The need for the pressure controller is apparent as prior to the controller test, the input pressure drifted by approximately 8 mmHg over the course of the hour, despite a constant input pressure being provided by the centrifugal pumps. Despite this, the results suggest that the system has the capability of successfully perfusing a porcine liver. Fig. 6 shows a comparison of the liver before and after perfusion. The deeper colour shown in the figure below indicates the presence of oxygenated blood throughout the liver. Some portions of the liver could not be perfused and so did not change in appearance, as seen in the edges of the lobe. This is potentially due to micro clots in the vasculature. It was determined that input pressures lower than 15 mmHg could not be tested as the system struggled to overcome pressure gradients to maintain blood flow. Additionally, advice provided by on-site clinicians suggested that sudden or large changes in pressure could damage the liver by rupturing capillaries which, in turn, would affect the results from the experiment.

Machine perfusion has been shown to be invaluable in clinical practice, however, has been too costly for research purposes. For example, the Organ Ox Metra costs approximately £30,000 per device per year on lease and uses single-use consumables, adding to the overall cost (approx. £6,000). By providing an alternative, low cost (approx. £11,000), reusable, adaptable research platform, the system can assist researchers in continuous monitoring and control of several key functional parameters relevant to their respective discipline or area of interest. Our results demonstrate that whole ex-vivo organ perfusion with this system is feasible and a promising alternative to current commercial perfusion devices. Our perfusion circuit continues to be developed with the addition of other sensors and controllers as per the requirements of individual experiments across multiple clinical research areas. Further work on additional porcine livers continues to be conducted to test the system. Furthermore, work to assess the quality of the perfusion using multispectral imaging techniques and functional liver tests are in progress with promising initial results. Additionally, work is underway to utilise the system to test a new loco-regional ablation treatment on ex-vivo perfused human organs, which will further demonstrate the versatility and research contribution of the research organ perfusion system.

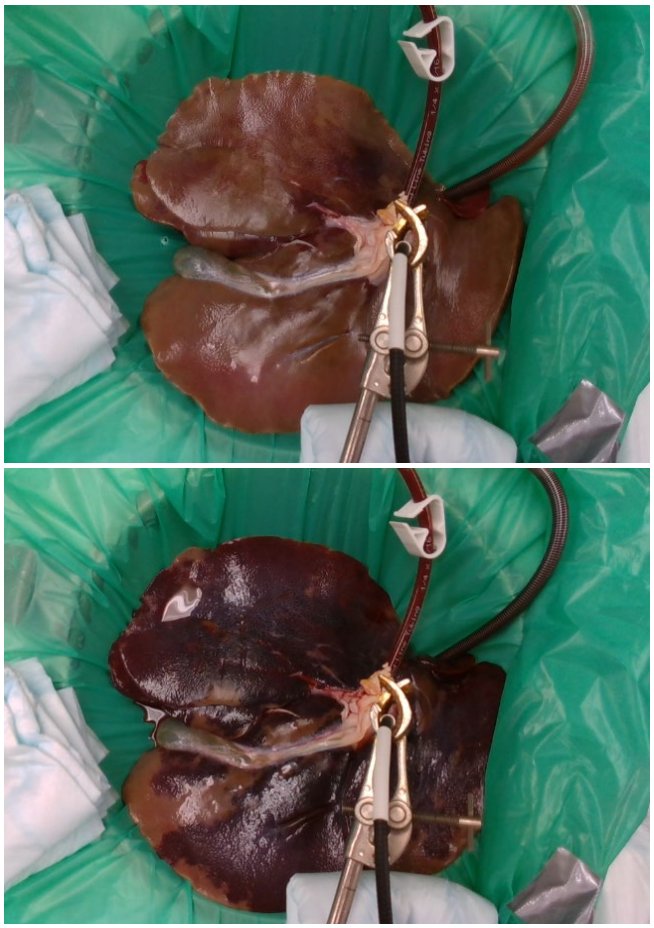

*Figure 6: Figure shows before (above) and after (below) the perfusion experiment. The liver is fully perfused and maintained stable flow into and out of the major vessels.*

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