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Title: 3D Printing system for cartilage tissue engineering

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Introduction:

One of the aims of the Christchurch Regenerative Medicine and Tissue Engineering (CReaTE) group is to repair damaged or diseased human musculoskeletal tissues such as cartilage or bone by combining patients' cells (e.g. stem cells) with degradable biomaterials in order to generate new functional tissues. Porous biomaterial scaffolds are central to tissue engineering strategies since they provide a carrier for cells, and are responsible for promoting reparative tissue formation.

The CReaTE group has developed cutting edge 3D Printing technologies. Their in-house and commercial 3D BioPrinting machines are capable of printing biodegradable polymers, cells or micro-tissue units. Micro-tissues are small (1mm diameter) spheres consisting of human cells, grown in the lab which can be seeded, or placed, into a porous 3D printed scaffold. A prototype micro-tissue handling system has been developed to aid in the seeding process. The automated handling system is designed to singularise micro-tissues. This is so that large numbers of micro-tissues can be individually selected and inserted into the scaffold without the micro-tissue being damaged. The singulation device uses fluidic valves connected to cell media under positive and negative (vacuum) pressure. These valves can be controlled electronically to add or remove media from the designed singulation chamber enabling the capture and then release of individual micro-tissues.

Aim:

The overall aim of this project was to use bioengineering and mechatronics principals to make further progress into developing a fully integrated and automated system capable of 3D printing scaffolds and inserting live micro-tissues into the scaffolds. Initially the singulation device had to be reconstructed and tested in order to determine what improvements needed to be made. From this the following key objectives were defined:

- Optimise and automate the singulation device
- Develop a micro-tissue sensing method
- Integrate the singulation device onto the 3D printer head
- Establishing a communication pathway between the singulation device control system and the 3D printer

Methods:

In order to control the singulation device, a LabVIEW based controller was used. LabVIEW is a software tool that uses a graphical programming language to program a microcontroller. A large amount of time was spent developing LabVIEW code in order to make the system function correctly. The system also had to be automated so once an external start command was received, a single micro-tissue would be delivered.

The sensing system was designed to detect the micro-tissue leaving the singulation chamber and travelling to be seeded into the scaffold. It was implemented with a simple photo-interrupter circuit that produced an electrical pulse whenever a micro-tissue passed through the sensor. This pulse was detectable by the microcontroller and software was used to process and display the results to the user.

To ensure the sensing circuit worked reliably, it was tested by passing 100 micro-tissues though it and recording any failures.

Integrating all the components of the singulation device onto the tool head required modification of numerous components to fit within the space confines of the 3D Printer. The Perspex blocks containing the fluidic valves were modified to add screw holes so it could be securely mounted, and the block was altered into a manifold to minimise the number of connections required which saved space. Some components were also 3D printed to allow other components, such as the hopper, to be mounted in optimal locations.

Communication between the singulation device and the 3D printer enables the printer to ask the singulation device to seed a single micro-tissue and for the singulation device to reply with any errors. The intention was for this to be conducted using the spare inputs and outputs available on the 3D printer and to be interfaced to the singulation device controller. The interface between devices would be electrically isolated to prevent damage in the case of faults.

Results:

Improvements implemented during this project mean the system now operates more reliably from a software perspective. The control loops maintaining constant positive and negative pressure are significantly more stable and work over a larger range of input pressures. The system is fully automated and has software routines to automatically clear blocks and alert the user if the singulation process fails.

The results of testing the sensor system indicate it is highly reliable with a 96% success rate. The four failures were cases where the system detected two micro-tissues instead of one. Further investigation indicates this is probably due to air bubbles leading or following the micro-tissues. The source of the air bubbles has been determined and replacement seals have been ordered.

Mounting all the components of the singulation device onto the printer head was a success. All the components fit well and the head fits within the docking station. The tool changer can successfully pick up, replace, and move the tool head without problems.

The communications system needs further work for it to interface and control the spare input and output pins correctly. In the meantime, we have developed a temporary method that allows for single direction communications to allow the printer to request a micro-tissue. This is currently in the testing stage.

Conclusion:

Significant progress has been made with the project. The singulation system is now fully automated and mounted onto the print head. The communications between the devices will allow true automation; where a whole scaffold can be printed and seeded with the press of a single button. These developments mean that we are close to realising our capability for the fully automated 3D Printing and assembly of micro-tissues to form advanced tissue engineered grafts to repair patient's damaged or diseased cartilage and bone.