Designing a Single Cell Selection and Placement Device for 3D Printing

Ethical Barriers and Their Implications in 3D Printing

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By

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On my honor as a University student, I have neither given nor received unauthorized aid

on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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Organ Transplants: Fixing a Broken Supply Chain

Of all the problems that exist within the field of organ transplantation, the shortage of available organs is by far the largest. There are currently over 100,000 people on the waitlist for organ transplants, and average wait times can be upwards of 3 years ("The Kidney Transplant Waitlist – What You Need to Know | National Kidney Foundation," n.d. n.p.). This problem has deadly consequences; in addition to the myriad chronic health problems and quality of life issues that plague patients waiting for organs, 17 people die everyday waiting for an organ ("Organ Donation and Transplantation," n.d. n.p.). The availability of organs is limited by several factors. Most organs come from deceased donors and less than 3 in 1,000 registered organ donors die in a way that their organs can be preserved and transplanted ("Organ Donation and Transplantation," n.d. n.p.). Additionally, the antibodies of the donor must match with that of the recipient for an organ transplant to be successful, and there is a very limited window of time in which an organ can be transplanted after a donor dies before it becomes unusable (Saidi & Hejazii Kenari, 2014, n.p.).

In an attempt to remedy this shortage of available organs, the capstone project outlined in this prospectus will deliver a cell selection and placement device that can be integrated into the rapidly advancing 3D printing field. Additionally, my capstone team will analyze and prepare a report on any potential ethical barriers that could conflict with our device's implementation.

In less than a decade, 3D printing has gone from being a crude, expensive process to a refined, rapidly developing technology that is used for everything from making bicycle parts to rocket engines (Murphy & Atala, 2014, n.p.). Despite this progress, 3D printing still has not realized its full potential. The next step of 3D printing could take it to the biomedical field, because 3D printing and automation have just now reached a level where they could potentially

have implications for bioprinting and artificial tissue constructs. Streamlining the automation user interface and other specifics could lead to a revolution in the artificial organ field. However, if the current situation stays the same, then 3D bioprinting will likely remain relegated to human work intensive, simple tissue constructs and we will miss out on the possibility of manufacturing artificial organs (Bhattacharjee, Urrios, Kang, & Folch, 2016, n.p.).

I propose that these new technological opportunities be taken advantage of and integrated into new technology that could print artificial organs. My capstone team will explore these opportunities by designing an automated cell selection and placement system which will then be incorporated into existing 3D printing technology. This device, although just a step forward, will lay the foundation for future designs that incorporate computer vision in order to identify, select, and move target cell clusters automatically, and will enable 3D printing devices to seed cells into 3D printed scaffolds. If successful, in the future, organs could be printed on site, using the patient's own cells; this would provide an unlimited supply of organs that would be available for immediate transplantation.

Designing a Single Cell Selection and Placement Device for 3D Printing

There is currently a lack of any device on the market which is able to manipulate and place complex cell clusters; this is a problem that the device being constructed by my capstone team hopes to resolve. The aims of this project are threefold. Firstly, it will seek to recreate an open-source manual micromanipulator that is capable of aspirating polymer microspheres, which are microscopic, plastic-like beads (Grexa et al., 2021, n.p.). Secondly, we will develop a computational framework that is able to precisely control step motors able to both position the device and operate the aspiration mechanism. Finally, we intend to implement both solutions to

successfully aspirate and move cell clusters to a target location intact. An overview of the automated cell selection and placement process is illustrated in Figure 1.

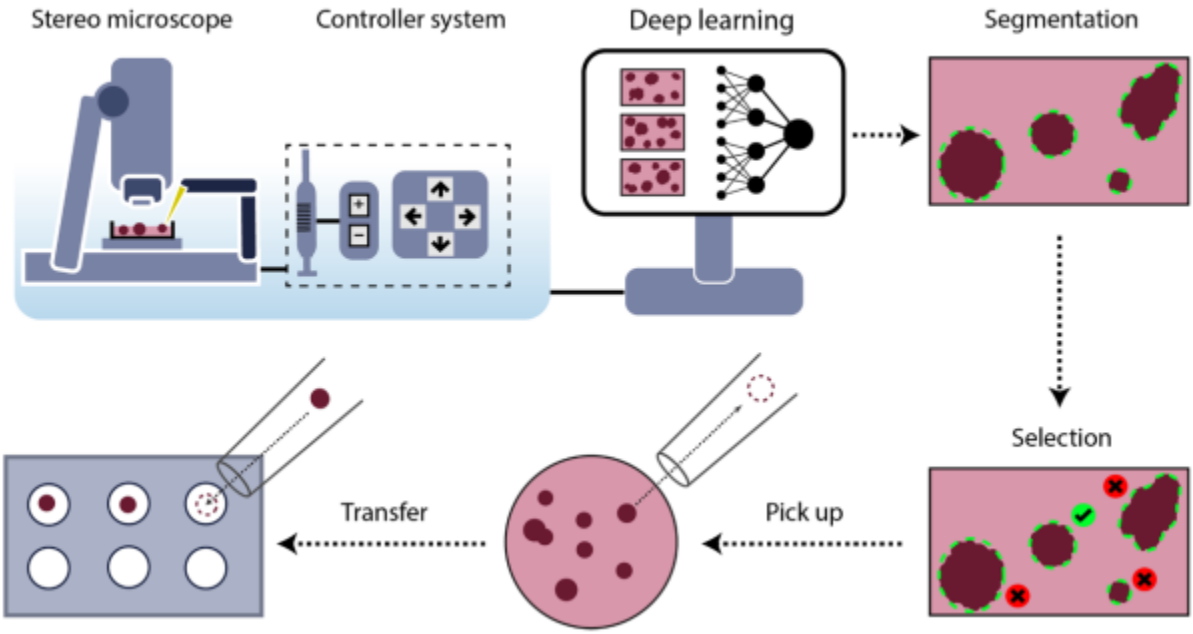

Figure 1: The outline of the cell selection process is shown above. Individual cells or cell clusters will be selected from a source and then placed in the target location (Grexa et al., 2021, n.p.).

Our project will be built on existing stepper motor and aspirator technology. The physical design of our project will consist of two separate parts. The positioning aspect will consist of two stepper motors mounted on rails, orientated in the X-Y plane as shown in Figure 2.

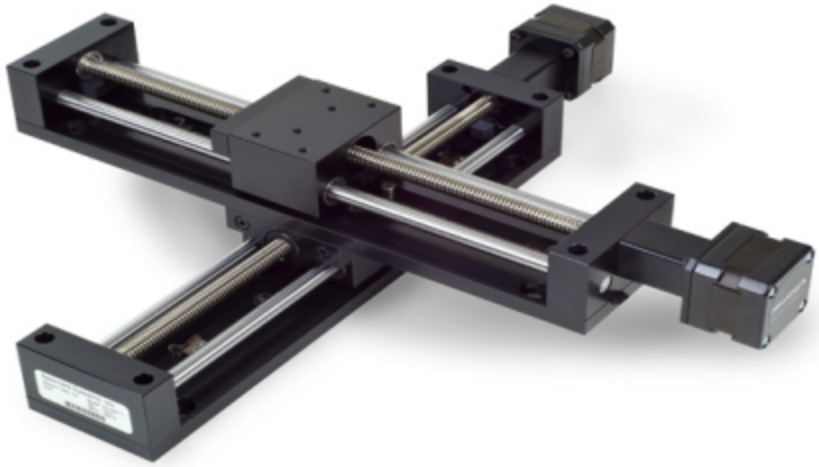

Figure 2: An example of two rail mounted stepper motors, orientated in the X-Y plane, is shown ("eTrack Low Cost Linear Stage," n.d. n.p.).

This will enable the device to position itself in the appropriate location above the culture plate it is selecting cells from. The selection and placement aspect will consist of a pulled glass capillary that is attached to a third rail mounted stepper motor orientated in the Z plane (up and down). This will enable the device to aspirate and place single cells or cell clusters into their target location. Many of the complications in this project will come from how small the cell clusters we will be working with are. This requires every component of the device to perform within very precise specifications. To accurately target single cells, our stepper motors will have to have a distance tolerance of less than 25 microns (Xu, Du, Liu, Kou, & Chen, 2021, n.p.). Additionally, the glass aspirator used to physically select and interact with the cells will have to perform with 100% efficiency due to the small amount of cells that we will be working with, meaning that no amount of cells can stick to it. This will be accomplished using special, superhydrophobic glass detailed in "Superhydrophobic Aspirator" (Guo et al., 2015, n.p.) . This glass is specially engineered so that nothing will stick to it on a molecular level, meaning that any cell picked up by this device will reach its target location.

Our device will be automated and controlled with a Simulink Matlab controller. This will enable it to work independently of a human operator and complete time intensive sets of customized selections automatically; this will solve a large problem in the 3D organ printing field, which is the large amount of human supervision and time needed to complete such a task (Schubert, van Langeveld, & Donoso, 2014, n.p.).

To accomplish its goal advancing 3D bioprinting technology, our device will also draw upon artificial scaffold and pluripotent STEM cell research as stated in 3D Bioprinting for Engineering Complex Tissues; "Combined with recent advances in human pluripotent stem cell technologies, 3D-bioprinted tissue models could serve as an enabling platform for high-throughput predictive drug screening and more effective regenerative therapies (Mandrycky, Wang, Kim, & Kim, 2016, n.p.)." One problem is that 3D printing full, functional organs may be too far off into the future to be addressed in the scope of this project. However, exploring this technology could develop simpler, but still very effective deliverables in the near future such as organs on chips. Organs on chips are artificial living organs that mimic the complex and physiological responses of real organs (Yi, Lee, & Cho, 2017, n.p.). We believe that meeting the above objectives will be sufficient to produce a functional automatic micromanipulator capable of being used in a lab setting. This device will enable 3D printers to seed complex cell clusters, instead of just printing with a homogenous biocompatible ink while enabling more consistent and rapid development of engineered tissues *in vitro* by reducing the need for human inputs

Ethical Barriers and Their Implications in 3D Printing

There is a considerable ethical problem with artificial organs. Many people have religious or ethical beliefs with certain medical procedures, including organ transplants and blood donations. Another issue is that any disability or condition that could be treated is not always seen as a condition to be fixed by people affected by it. For example, new treatments for restoring hearing can be seen as threatening the very existence of the deaf community. As stated in Implant Ethics, "One form of implantation, namely cochlear implants, has been heavily criticised by members of the Deaf community for undermining their very existence (Hansson, 2005, n.p.)." Additionally, fears have been expressed that non-voluntary interventions may be carried out, perhaps in the form of brain implants used to control other human beings .

Our team must figure out how religious or ethical concerns will be overcome when trying to introduce this revolutionary new technology (Hansson, 2005, n.p.). Failing to address this issue could lead to difficulties in this technology being implemented and will result in many more deaths while patients wait for organs and will cost the healthcare system a significant amount of money from the loss of cheaper treatments. Increasing public awareness of the safety, as well as the current alternatives to a treatment such as this, which are few and far between and usually include accepting a chronic, disabling condition, could lead to a successful resolution of this problem. A patient that is facing a deadly, indefinite wait for a donated organ may opt for an artificially printed organ despite their own ethical problems with it. This, however, will require additional surveys and research on the public opinion directly related to this technology.

Finalizing Our Goals

Once our team completes our capstone project, we plan to have several specific deliverables. The technical deliverable will be an integrated, automated, cell selection and placement device that will potentially have attachments to streamline its integration into current

3D printers, allowing for the efficient construction of complex tissues. The STS deliverable will be a compiled list and explanation of the anticipated ethical concerns with artificial organs and what possible resolutions could exist. These deliverables will provide a stepping stone for future advances in 3D printed organs, and an immediate solution that could be implemented in making miniature organs such as organs on chips or smaller bioprinted tissue constructs. Once this technology is further developed, it will lead to revolutionary advances in the field of organ transplantation, and will provide a near limitless supply of artificial organs to alleviate the current shortage. The resulting STS research on ethical concerns will provide a clear framework on how to navigate the surrounding ethical concerns once 3D organ printing technology is advanced to an applicable level.

Word count:1586 (1730 revised) All boxes corrected; I have attached a PDF in which all of the changes made are detailed, this is the original revised version

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