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Qualifier Question: 3D printing of human organs for are expanding rapidly in medical applications. In fact, they are expected to revolutionize healthcare. Research 3D printing of human organs and relate your findings into your project.

Tissue engineering is a relatively new field whose ultimate goal is implantation of tissue constructs for injury repair or organ replacement (Berthiaume , et. al 2011)[1]. Tissue engineering is based on three approaches: biomimicry, autonomous self-assembly and mini-tissue building blocks (Murphy and Atala, 2014)[2]:

- Biomimicry: The design, manufacturing and production of materials, structures, and identical functions - cellular and extracellular- of tissues or organs
- Autonomous self-assembly: Replication of biological tissue using embryonic organ development as a guide.
- Mini-Tissue: Use of the smallest structural and functional components of tissues and organs to self-assemble into macro-tissues.

Source: Murphy, Sean V., and Anthony Atala. "3D bioprinting of tissues and organs." Nature biotechnology 32.8 (2014): 773.

Precise measurements and exact functionality then are paramount to the making of useful tissues and organs. Bioprinting follows three steps: pre-bioprinting, bioprinting, and post-bioprinting. Pre-bioprinting, the step I will be focusing on for this paper, involves imaging and digital design in addition to material selection (Shaifee and Atala, 2016)[3]. This step usually includes computed tomography (CT) and magnetic resonance imaging (MRI) to image the organ or tissue followed by tomographic reconstruction to better understand layer by layer fabrication and achieve segmental 2D images. Stereolithography files (STL)- which describe the surface geometry of 3D objects- makes use of these preparations to create the 3D representation of the organ or tissue. Material selection, and the biological process for which tissue engineering is based on, is next selected.

The imaging and digital design aspect of tissue engineering includes additional complexities requiring careful consideration of composition and organization of the organ or tissue components. Computer-aided design and computer-aided manufacturing (CAD-CAM) tools are used to collect and digitize the architectural information of tissues (Murphy and Atala, 2014). The volume of the tissue, to make up the 3D model representation, is carefully made and described by these image sources, as well as X-ray, to render the surface and all aspects

[1] Berthiaume, François, Timothy J. Maguire, and Martin L. Yarmush. "Tissue engineering and regenerative medicine: history, progress, and challenges." *Annual review of chemical and biomolecular engineering* 2 (2011): 403-430.
[2] Murphy, Sean V., and Anthony Atala. "3D bioprinting of tissues and organs." *Nature biotechnology* 32.8 (2014): 773.
[3] Shafiee, Ashkan, and Anthony Atala. "Printing technologies for medical applications." Trends in molecular medicine 22.3 (2016): 254-265.

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regarding the tissue. Images or models can be viewed in a variety of ways, including contour stacks, wire-frame models, shaded models, or solid models with variable transparency, lighting and reflectivity (Sun and Lal, 2002)[4].

Our project objective is, similarly, to create a 3D simulation model of the liver. The application would adapt according to a patient's Electronic Health Record (EHR), changing from a healthy liver to a compromised liver depending on the diagnosis the patient has. Our implementation process is likely to involve the use of Unity, a platform game engine used to create 2D and 3D games and simulations. While, as a group, we will be exploring the process as we are all quite new to animation, the process happens to be quite similar to the 3D pre-bioprinting process. Creating a model involves manipulation of axis in position, rotation and scale according to the human dimensions of a liver (which, thankfully has already been extensively studied so we won't need to study an actual liver in real time!). Unity provides an interface for manipulating the axis at different points to create the object- the trick then is figuring out the layering that would correctly simulate the state of the liver. Here, extensive research will be made to research the differences of an unhealthy liver against a healthy liver and simulate that for the benefit of patient education.

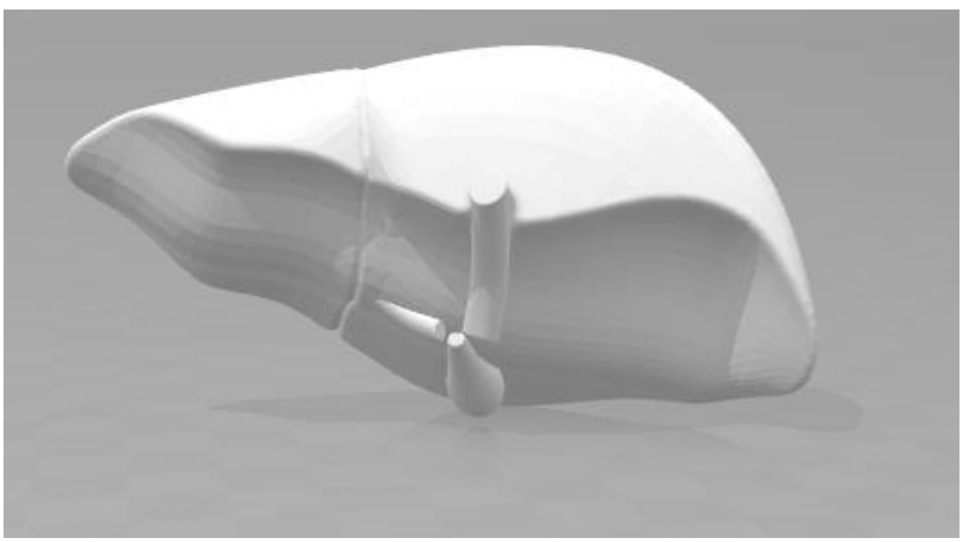

Fig 1. Liver object created using axis manipulation according to an anatomical diagram. We will be using this object in Unity.

The most challenging aspect will be to carefully add different materials, textures and shaders to the liver object, shown in Figure 1, as assets to the object. The materials and textures will need to precisely match the *look* of the disease and we plan to use different medical resources, such as human anatomy Atlus- a collection of anatomically correct images of

[4] Sun, Wei, and Pallavi Lal. "Recent development on computer aided tissue engineering—a review." *Computer methods and programs in biomedicine* 67.2 (2002): 85-103.

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organs and different disease states. With this we will create a material to describe a property, such as a color, and textures and shaders will dictate which properties, and which textures a material can have. Layering these materials on to each other will eventually produce the desired image, rendered in 3D, with the added benefit of changing from healthy liver to diseased liver using a script coded via FHIR resources.

Using unity as we are obviously pales in comparison to the process in creating an actual usable organ as in 3D bioprinting, but the end rendering of the first step is the same in that both processes aim to create an accurate 3D representation of the organ. These printed models, apart from being the base model for which an actual organ tissue is evaluated with, have also traditionally served as medical education tools for professionals, clinicians, and patients alike. Patient education has been difficult because often diseases and illnesses are abstract in nature and because of this patient are unlikely to adhere to or completely understand anatomy, physiology, disease characteristics, surgery and surgical risks of diseases and illnesses. Naturally then, tailored 3D printing of organs for the purposes of education has been beneficial in this educational realm- in a study by Yang et al "The Impact of using Three-dimensional printed liver models for patient education", investigators set out to create patient-specific liver models using resin for children with hepatic tumors scheduled for hepatectomy (Yang et. al., 2018)[5]. In this study, seven children and their parents were enrolled and presented with 3D printed models of their specific child's liver condition and where then given a questionnaire assessing their understanding before and after given the model with information regarding the anatomy and physiology, tumor characteristics, surgical intervention, surgical risks, and outcomes. The process of printing the organ followed the same pre-bioprinting process described before- requiring a CT scan among other imaging techniques to render the personalized rendition of the patient's liver.

Supporting the idea of patient benefits of the model, results of the study suggested a significant patient understanding of basic liver anatomy and physiology, planned surgical procedure and surgical risks. The mean improvement, empirically was "26.4% in their understanding of basic liver anatomy, 23.6% for basic liver physiology, 21.4% for tumour characteristics, 31.4% for the planned surgical procedure, and 27.9% for surgical risks. The overall improvement was 26.1%" (Yang et al, 2018). Reassuring the patients (particularly the parents in this study) is indispensable since, understandably, the comforting aspects of being informed gives the feeling of being more involved and informed in the decision-making process of surgical intervention for their children. 3D printing and imaging becomes beneficial in enhancing imaging work, such as the field of radiology, for the benefit of improving patient care and enhancing the relative contribution of care by radiologists (Ballard et al, 2018)[6].

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[5] Yang, Tianyou, et al. "The impact of using three-dimensional printed liver models for patient education." *Journal of International Medical Research* (2018): 0300060518755267.
[6] Ballard, David H., et al. "Clinical applications of 3D printing: primer for radiologists." *Academic radiology* 25.1 (2018): 52-65.

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Radiologists are interested in delivering personalized care based on the patient's anatomical data- information that they require and work with daily. In addition, 3D models are transforming medical education by way of anatomy teaching and operative rehearsal. 3D printing and 3D modeling, such as in the project we have proposed, have extensively supplemented anatomy education by creating a reproductively practice environment. According to Trace et al, benefits are "i) models are reproducible and safe to handle and ii) models can be created from a wide variety of imaging sources representing normal and pathological anatomy" (Trace et al, 2016)[7].

In accordance then to the current usage of 3D printing and imaging, we hope that our project can be seen as beneficial to the current landscape of patient education. While there are certainly many resources for anatomical modeling in the 2D and 3D space, we hope that the added benefit of creating the simulations on demand based on the patient's own pathological data and disease state becomes beneficial to the understanding of their health state, as has been seeing in the studies discussed in this paper.

Resources:

[1] Berthiaume, François, Timothy J. Maguire, and Martin L. Yarmush. "Tissue engineering and regenerative medicine: history, progress, and challenges." *Annual review of chemical and biomolecular engineering* 2 (2011): 403-430.

[2] Murphy, Sean V., and Anthony Atala. "3D bioprinting of tissues and organs." *Nature biotechnology* 32.8 (2014): 773.

[3] Shafiee, Ashkan, and Anthony Atala. "Printing technologies for medical applications." Trends in molecular medicine 22.3 (2016): 254-265.

[4] Sun, Wei, and Pallavi Lal. "Recent development on computer aided tissue engineering—a review." *Computer methods and programs in biomedicine* 67.2 (2002): 85-103.

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[6] Ballard, David H., et al. "Clinical applications of 3D printing: primer for radiologists." *Academic radiology* 25.1 (2018): 52-65.

[7] Trace AP, Ortiz D, Deal A, et al. Radiology's emerging role in 3-D printing applications in health care. J Am Coll Radiol 2016; 13:856–862, e4. doi:10.1016/j.jacr.2016.03.025.

[7] Trace AP, Ortiz D, Deal A, et al. Radiology's emerging role in 3-D printing applications in health care. J Am Coll Radiol 2016; 13:856–862, e4. doi:10.1016/j.jacr.2016.03.025.