Natural and Synthetic Supporting Structures for the Perfusion of Hydrogel Constructs
(Technical Paper)

Effects of Emergency Medical Care Network on Different Groups of People
(STS Paper)

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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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Introduction

Many patients experiencing end stage organ failure will only have two choices of treatment options. The first option consists of an organ transplant and the second option is to opt for conservation care in order to manage the disease symptoms (Mayo Clinic, 2021). Most clinicians will refer the patient to be added on the organ transplant list rather than conservation care due to the fact that people who receive a donated organ will have a greater chance of living a longer life than those who are not able to receive one (NIH, 2021). However, organ transplant is experiencing a major shortage crisis as the available viable organ does not meet the existing demand of the public (ScienceDirect, 2020; PubMed, 2008). Every 9 minutes another patient is added to the organ transplant waiting list and around 17 people die each day waiting for one (HRSA, 2021).

The tissue engineering field aims to address this problem by focusing on creating functional substitution for damaged tissues (Rouwkema et al., 2008). However, a challenge preventing advancements within the tissue engineering field is incorporating blood flow (vasculature) to different tissue constructs outside of the body (in-vitro) in order to maintain a viable environment for the cells and allow tissue regeneration. Researchers are currently integrating a perfusion device and chips to support fluid flow for the in-vitro vascular system (Bancroft et al., 2003; Wang & Shuler, 2018). There are limitations to this approach as the complexity of creating these devices prevents researchers from producing it effectively in a timely manner. Additionally, these perfusion devices cannot integrate blood vessels and engineered tissues within the body (in-vivo) through a complete connection. Thus, the technical project aspect will first focus on creating a three-dimension (3D) bioprinted synthetic perfusion device that will enable a connection to a flow generating machine in order to provide vasculature. The second focus is aimed towards developing a new process to create a physical connection between engineered tissues to biological tissues.

Technical Project

The body relies on blood vessels to diffuse oxygen and nutrients as well as disposing waste between the cells. Therefore tissue engineering research focuses on incorporating vasculature for all tissue-engineered constructs. The addition of vascular networks will enhance the tissues ability to perfuse and perform cell functions needed for survival. Tissue experiencing insufficient vascularization will gradually become nutrient deficient and hypoxic, which in turns will decrease tissue functions and potentially cause cell death (Rouwkema et al., 2008). Due to the importance of vascularization and the need for perfusion within tissues, hydrogel has become an emerging material used in this field (Liu et al., 2021).

Hydrogels are insoluble water-swollen networks used primarily in biomedical applications (Burdick & Stevens, 2005). It is becoming more widely used within the tissue engineering field as it consists of a wide range of applications. The polymer of a hydrogel can be constructed from a numerous type of materials along with being able to be formed using many different processes and mechanisms (Burdick & Stevens, 2005). Properties of a hydrogel can be advantageous when used as a biomaterial by allowing tissues to incorporate certain mechanical characteristics, achieve desirable degradation rate and integrate swelling physical properties. Overall, it can be manipulated and tailored to a specific application by obtaining certain physical properties and biological properties such as creating the vascular network within a tissue. However, there are limitations when utilizing hydrogels as the mechanical properties inhibit proper connection for perfusion and hinder the diffusion needed for cell survival.

The first part of the project aims to create a synthetic perfusion device that will house the hydrogel and enable connections for perfusion throughout the tissue. The advancement in bioprinting has led to the development of 3D printed vascular tissue for both in-vitro and in-vivo application (Chen et al., 2021). Therefore the same technology can be applied in developing a perfusion device using synthetic material such as polydimethylsiloxane (PDMS). PDMS is a type of hydrophobic polymer which provides a more stable and rigid structure than a hydrogel thus could potentially act as the perfusion connection (Xu et al., 2021.).

Utilizing the bioprinting technology, PDMS will be 3D printed into a perfusion chip that will encapsulate a hydrogel, more specifically for our project, an engineered tissue made from norbornene-modified hyaluronic acid (norHA) (Kolesky et al., 2016). From there, channels will be integrated by implementing 3D printing sacrificial ink (McCormack et al., 2020). The device then will incorporate connections to a flow-generating machine such as a peristaltic pump. Lastly, the device will facilitate confocal microscopy by the addition of a glass sheet cover.

The second part of the project aims to research the possibility of making a new process to create physical adhesion between engineered tissues and biological tissues. Accomplishing this goal will allow the ease of implanting bioengineered tissue within any parts of the body and be used as a treatment later on. The project will consist of applying a chemical modification to norHA which will add aldehyde groups to the hydrogel. From there, the modification will allow a connection to be made with BAM, a bladder acellular matrix which is known as a decellularized pig's bladder. The whole process will yield a hybrid material consisting of an engineered tissue (norHA) and a biological tissue (BAM).

Emergency Medical Treatment

Newer options for treatments and care become accessible to the public that aim to improve the healthcare field and increase the population's life expectancy (Medicine (US), 2008). However, there are still shortfalls within the system causing many to believe that healthcare is a luxury for the rich and not for all who seek it. An example to display this particular problem is the use of emergency medical service (EMS) outside of the hospital. Places where EMS is widely available and healthcare insurance is accessible to the majority, will have a higher number of users than places that lack those elements (Tärnqvist et al., 2017). Because of that, some will inappropriately use this system and drain healthcare resources (Dejean et al., 2016). The imbalance of healthcare around the world determines who can and can't use this service.

The aim is to explore the use and availability of EMS for pre-hospital treatments along with the impact it has on the society. The interactive sociotechnical analysis (ISTA) framework will be used to compare and contrast the interaction among subcomponents of a sociotechnical system (Harrison et al., 2007). The interactions between these groups will reveal sources of unintentional consequences relating to EMS. There are five types of interaction that will be discussed; implementing new EMS to existing social systems, technical and physical infrastructures that mediates EMS use, social systems that mediates EMS use, effects of present EMS on the social system and interaction of new EMS changes with the present EMS.

The first type relates to places where EMS is limited or nonexistent. Many places lack the ability to fund a system where trained personnel can respond to the community's needs. However, different organizations such as WHO, UNICEF, and the World Bank have been intervening health programs all around the world to develop a set of basic emergency care services (The World Bank, 2019). This is able to serve as a key component to the overall health of the population. A study was shown where the implantation of a new EMS was able to increase access to hospital care for its citizens but it also significantly increased hospital admissions (Caviglia et al., 2021). Thus resulting in an imbalance of available resources. Despite the low funding and resources available, the use of an EMS system was able to lower mortality rates amongst different classes of people (J. A. Razzak & Kellermann, 2002).

The second type compares the infrastructures that affect how EMS can be used. There's an overwhelming amount of infrastructures of all kinds that impacts countries with low to middle-income and prevents it from successfully achieving prehospital care (Kironji et al., 2018). The most impactful barrier found through a systematic review that these countries experience is transportation deficiency, lack of trained providers, lack of equipment, lack of financial resources and limited communication along with coordination amongst healthcare facilities (Kironji et al., 2018). All of which causes a delay in the development of EMS care. It could also prevent certain groups of people from using it as the cost will be too high or if the service is not available in the area they live.

The third type shows how a social system in place could regulate how EMS is used. Some countries are able to provide EMS care to its communities; however, the public isn't always satisfied with how it's being provided or what is being provided (J. Razzak et al., 2008). Pakistan is an example where the majority of community respondents voiced dissatisfaction with the emergency care service while the majority of the community leaders were satisfied (J. Razzak et al., 2008). Further details showed that the expenses were too high, therefore, many tend to go for the public sector rather than the private sector. From here it was found that public sector facilities were not adequately equipped to treat emergencies, lacked personnel within the emergency department and overall emergency care did not function properly within the Pakistan government as no budget was allocated for this purpose. Therefore, the availability of EMS within that social system did not benefit the majority of the community.

The fourth type analyses the current EMS system and the relation it has to the social system. Places where resources are abundant, in terms of having insurance coverage for most of the communities, the education available for the first responders and the corresponding facilities equipped with the care needed, will be most efficient and allow its community to rely on them. Thus those living there will call for help when needed or not and trust that the EMS system will take care of them. However, other places who lack the resources will end up not having the resource available to use and will then rely on themselves for care. Those people would rather use home remedies than to put their trust in the system. It's imperative that some of the problem is placed on the inadequate emergency care and the poor access to quality hospital care (Kobusingye et al., 2006).

The fifth type analyzes how new changes within the EMS system affect the current EMS system. The EMS system has been developing and advancing through a very slow process. It wasn't till the early 60s where changes began to develop a more structured EMS system (Shah, 2011). As more data and research comes in, it slowly incorporates itself in. However, this is not always the case as EMS lacks the uniform regulations and standards (Kobusingye et al., 2006). Therefore, new changes are only implemented when its deemed to be necessary. Overall, there are many interactions between different groups that affect how EMS is operated. Certain aspects would result in a predictable outcome while others would not. Thus it could generate unintended consequences.

Research Questions and Methods

This project's focus will be based on the following questions. How will the EMS system be compared from all around the world? From those comparisons, examine how the EMS system is affecting the society and if implementing new EMS is plausible in those areas that lack this service. If it is, what changes will be devolved within its social system?

Trek Medics International for emergency and ambulance service databases will serve to obtain statistical data on the available EMS service in different countries/regions (Trek Medics

International, 2021). Different research papers will review EMS systems in a variety of countries such as those in North America, Africa, Europe, Asia, and the Middle East (Page et al., 2013; Roudsari et al., 2007). It will also serve to pinpoint places with available EMS and places without it. The economy based on GDP will be compared amongst countries along with the education available and the population growth (World Population Review 2021; Worldometer, 2021). Rankings of healthcare will also be incorporated in (World Population Review, 2021). The regulations and standards imposed on EMS based on the national registry of emergency medical technician will then be yielded to determine the limitations of each country (National Registry of Emergency Medical Technicians, 2021). Lastly, interviews from currently and past EMTs based on the changes they have experienced along with the impact they have seen.

Conclusion

There are many limitations in creating vascularization in order to perform perfusion through engineered tissues. Therefore the technical project will aim to create a 3D printed synthetic perfusion device in order to provide the research field a tool for further innovations. However, the device will not have the ability to translate towards the treatment route. Thus, the second part of the project will work towards the development of creating physical connections between an engineered tissue and a biological tissue. If the second part results in a successful product, it could possibly translate into clinical work.

As the population increases and more health issues rising, EMS for pre-hospital care is becoming increasing important for the well-being of the community. However, not all EMS system is created equal. Therefore, the ISTA framework will be used to discuss the differences between the EMS systems from all around the world and the effect it has on the society as well as the vice versa. All of which will be done through a series of questions and resources obtained via the internet along with interviews. The results will showcase the interconnected relationship that EMS has on the community as well as the unintentional consequences that it might have.

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