Polymeric Synthetic Oxygen Carriers for Transfusion at the Location of Injury

(Technical Report)

Disparities in Access to Emergency Care: The Intersection of Race and Rurality

(STS Research 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

Hemorrhagic shock is a severe medical condition characterized by the lack of adequate blood flow caused from excessive blood loss. This typically leads to hypoxia which is the lack of oxygen delivered to cells ultimately resulting in cell death and organ failure (Cannon, 2018). In America, severe hemorrhage is the leading cause of death for people aged 46 and under. It is most often caused by physical trauma and particularly affects military personnel who suffer combat wounds (Cap et al., 2018). The current treatment for hemorrhagic shock is a whole blood transfusion. This process consists of administering healthy donor blood which contains hemoglobin, a necessary blood component that deliver oxygen to tissues. However, there are several issues with whole blood transfusion. First, blood is difficult to source due to reliance on donors and has stringent storage conditions both of which cause supply to be limited (Huish et al., 2019). Additionally, transfusion of blood can have adverse health effects such as an immune response caused by incompatible blood types or the introduction of bloodborne pathogens (Chambers et al., 2019). Therefore, there is a need for a safe, effective, and stable alternative for whole blood transfusions. The technical project is focused on creating a synthetic blood oxygen carrier to treat hypoxia resulting from severe hemorrhage and serve as an alternative to human blood. By overcoming the barriers associated with the current treatment, the project aims to improve the access of emergency transfusion technology to otherwise marginalized groups. Blood transfusions only represent a small portion of emergency procedures, so the STS project is aimed at uncovering the disparities in access to all emergency services across both race and rurality in the United States. It will inform the important sociotechnical considerations that must be made during the development of the synthetic blood oxygen carrier in the technical project, and, together, these projects will help improve the treatment of hemorrhagic shock for all people.

Technical Project

To circumvent the large volumes and strict storage conditions associated with human blood, the synthetic blood alternative will be designed to be a dried powder. The idea is that, at the site of the injury, the medical professional or military personnel can resuspend the dried powder in sterile water. Then, using standard transfusion practices, the reconstituted powder will be administered to the patient. There are several components of this dried formulation. The first of which is the oxygen carrying component: perfluorocarbons. Perfluorocarbons (PFCs) are small molecules that not only carry oxygen but are also biologically inert which makes them suitable for administration to the human body. Due to these unique properties, PFCs have been used in numerous medicinal applications such as cancer treatment, cell therapy, imaging, and, naturally, oxygenation of tissues (Kakaei et al., 2023). However, PFCs are not miscible in water, so they can't be directly injected into the body. Instead, they must be encapsulated within another material such as polymers (Spahn, 1999). With the help of surfactants and high energy, PFCs can form an emulsion in water where they are encapsulated by the polymer (Riess, 2005). Then, it can be dried using a process known as lyophilization where the emulsion is rapidly frozen and placed in a vacuum to allow the liquid to sublimate. The resulting dried formulation consists of encapsulated PFCs that range from approximately 200-500 nanometers in diameter making them nanoparticles.

These PFCs are tested *in vivo* using a murine hemorrhagic shock model where mice are first induced with hemorrhagic shock and then treated with the nanoparticles resuspended in water. The preliminary data suggests that the PFC formulations do, in fact, increase the dissolved oxygen concentration in the blood, but it causes a brief yet significant drop in mean arterial pressure that ultimately proves fatal for the mice. It is hypothesized that this is due to the size of the nanoparticles, and that decreasing the size can prevent the drop in mean arterial pressure. To investigate the effects of particle size on the survivability of the mice, the parameters of the nanoparticle synthesis protocol must be modified. First, during the emulsification process, a high amount of energy must be inputted into the solution. This is done through a sonicator which emits high energy sound waves. The amplitude, duration, and probe tip of the sonicator can be adjusted to increase the total amount of energy applied to the solution. Second, the organic solvent which is responsible for dissolving the polymer may cause larger particles to form. So, decreasing the amount of organic solvent used and increasing the rate at which it evaporates may cause the formation of smaller nanoparticles. Finally, the rate of freezing before lyophilization may also affect the size of the nanoparticles (Hernández-Giottonini et al., 2020). All these factors will first be tested using *in vitro* measurements: dynamic light scatter (DLS) to measure the size of the particles and a Foxy FOSPOR-R O_2 sensor to measure the dissolved oxygen capacity. Once the optimal synthesis procedure has been identified, the nanoparticles will be tested using the murine hemorrhagic shock model.

In conclusion, the technical project aims to improve upon whole blood transfusions as a treatment for hemorrhagic shock. If the product works as intended, the synthetic blood oxygen carrier will address the shortcomings of donor blood. The nanoparticles can me mass produced and easily stored without need for large volumes or refrigeration. Additionally, the dried formulation will only consist of the oxygen carrier, thus eliminating the chance for infection from bloodborne pathogens or an adverse immune response. All these benefits will translate to easier transport and distribution of the synthetic blood oxygen carrier. Hopefully, this will enable the widespread use of this technology resulting in an improvement in health outcomes for all patients who may experience hemorrhagic shock.

STS Project

To compressively understand procedures such as blood transfusions, one must first consider the sociotechnical factors that affect access to emergency services. One of these factors is race. According to many studies, racial and ethnic minorities receive lower standard of care, including in pain management, utilization of emergency medical services (EMS) during emergencies, and likelihood of being transported to a safety net hospital (Soares et al., 2019). Additionally, research shows that medical professionals often hold inaccurate beliefs about biological differences between Black and White patients which leads to disparities in pain assessment and, ultimately, treatment (Ventura et al., 2022). Another important factor to consider when understanding emergency procedures is rurality. A 2017 study showed that 29.7 of 309 million people in the United States were not within one hour of a trauma center, and people that lived in major cities and suburbs were significantly more likely to have access to a trauma center when compared to those in rural areas (Carr et al., 2017). Interestingly, the intersection between race and rurality also highlights unique problems with the emergency healthcare system. A ZIP Code Tabulation Areas (ZCTAs) analysis which measures the distances to the nearest medical services illustrated that rural high minoritized ZCTAs, specifically Black and American Indian/Alaskan Native persons, were significantly farther from hospital services than rural White ZCTAs. On the other hand, the opposite was true in urban areas where high minoritized ZCTAs were closer than non-minoritized ZCTAs (Eberth et al., 2022). In terms of quality of care, results of one study showed that, overall, non-white patients were more likely to receive a higher emergency severity index (ESI) score (meaning lower acuity) when compared to white patients. Moreover, in urban areas, this difference was statistically significant whereas in rural areas the difference was not as pronounced (Puissant et al., 2024).

Given the clear differences in proximity and quality of emergency care between both race and rurality, the STS project will aim to answer the following question: how is access to prompt, quality emergency medical care distributed between racial and ethnic communities in urban versus rural United States, why do they differ, and what are the outcomes of said treatment? To answer this question, the project will primarily employ an Intersecting Structures of Power framework. The specific structures of power that will be examined will be predominately race and rurality. However, it is also important to consider the healthcare system itself as a structure of power like in the *Born in the USA* film where directors Marcia Jamel and Ken Schneider utilize this framework to analyze the how the intersection between societal factors (race, economic status, education, etc.) and obstetric healthcare affected the quality of care and health outcomes for both mothers and infants (Jamel & Schneider, 2020). To uncover more about why these disparities may exist, a built environment analysis will also be performed. For example, some researchers suggest that proximity data, despite demonstrating that minorities are physically closer to emergency departments, does not reflect the barriers that they may face in urban areas such as reliance on public transportation (Eberth et al., 2022). A close inspection of the disparities in infrastructure surrounding both minority and rural populations may paint a clearer picture of the differences in health outcomes.

The project will be comprised of two main components. The first will be a deep literature review of the current disparities, causes, and outcomes associated with emergency medical care. This will provide an overarching view of the emergency healthcare landscape and provide a broader context for the second part of the project. The second part of the project will be a case study of the emergency services provided in the Charlottesville area. Specifically, this will involve an ethnographic investigation with trauma doctors, nurses, patients, emergency medical technicians, and paramedics across 9 rescue squads and 2 emergency departments in the area. By probing the experiences of the people involved in the emergency healthcare system, much can be discovered concerning the speed and quality of care as well as the existence of bias or discrimination in the system. To assess the built environment surrounding the Charlottesville area, the public transportation in the area will also be investigated. More specifically, its utilization demographics and accessibility in remote areas (e.g. frequency, stop locations) in relation to accessing emergency departments will be examined. This will elucidate reasons for disparities in emergency care.

This project will reveal the current state of the American emergency healthcare system in relation to the intersection of race and rurality. From this research, the areas of strength and weaknesses can be discovered. In turn, this will inform the research and design of future emergency health care services such as hospitals, ambulatory care, and more. Hopefully, this will result in a wider access to emergency care across all disenfranchised communities.

Conclusion

Hemorrhagic shock is a serious, life-threatening medical condition that affects almost anyone suffering from a traumatic physical injury. The technical project intends to improve upon whole blood transfusions as the standard of care by optimizing the production of dried-nanoparticle oxygen carriers. The STS project will analyze disparities in access to emergency care within both racial and rural versus urban communities through a literature and ethnographic review culminating in potential areas of improvement for the emergency healthcare system in the United States. In particular, it will provide valuable insight to ensure that the design and testing of the technical project is both equitable and effective. This fits in with the broader goal of the technical project which aims to expand the access and use of blood transfusion technology. The direct impact on human health will be an improvement on the health outcomes for all patients who may suffer from hemorrhagic shock.

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