Prospectus

Growth Factor Release from Microporous Annealed Particle (MAP) Hydrogel to Improve Wound Healing
(Technical Topic)

Disparities between Quality of Diabetic Care due to Income Differences
(STS Topic)

By

Meghan McDermott

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Technical Project Team Members: Regan Ellis, Lauren Pruett (PhD Candidate, Biomedical Engineering)

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.

Signed: _____ Date _____

Approved: Rider Foley, Department of Engineering and Society Date: December 10, 2019

Approved: Donald Griffin, Department of Biomedical Engineering Date: December 10, 2019

Introduction

Diabetes is a rising epidemic in the United States with the increased prevalence of obesity due to the amassing wage gap, which has prevented people from seeking proper healthcare (Riddle & Herman, 2018). Over 16 million people in the United States currently suffer from diabetes, a number that expands to over 200 million across the globe. The diabetic population is anticipated to be 366 million by 2030, globally (Margolis, et. al., 2011). This disease interests me as a couple of my family members have or have had Type II diabetes, the form often resulting from dietary habits, exercise habits, and often is in conjunction with hereditary predispositions (Centers for Disease Control and Prevention, 2019). In addition, witnessing the differences in approaches of their diabetic care between different family members due to financial insecurities has provided motivation for this research. The technical project of Growth Factor Release from Microporous Annealed Particle (MAP) Hydrogel to Improve Wound Healing that will be completed as the Capstone degree requirement in Biomedical Engineering will be the technical topic of interest.

This technical topic is related to the human and social dimensions that will be explored in the STS research paper because the technical project of MAP gel optimization can be applied to diabetic foot ulcer care. These chronic wounds that many diabetes patients develop, if not properly cared for, can result in limb amputations (Brem & Tomic-Canic, 2007). Therefore, as a possible emerging treatment for these dangerous wounds, similar to other emerging technologies, it is vital to consider how it will affect the entire diabetes patient population, including whether all income brackets will have access to this technology. I will focus on the effect of financial insecurity in diabetes care using the framework of techno-politics with an additional focus on the importance of inclusive innovation for the technical project.

Technical Topic

Between 10% and 15% of diabetes patients will develop or currently suffer from diabetic foot ulcers (DFUs). Diabetic foot ulcers can result from acute or chronic cutaneous disruptions to the skin, arterial complications, including cardiovascular blockages, peripheral neuropathy, or nerve damage, or a combination of these factors (Margolis, et. al., 2011). Patients with DFUs experience numerous resulting effects including decreased mobility, sleep deprivation, depression, anxiety and possible requirement of limb amputation (Pop & Almquist, 2017). Further, DFUs and their symptoms are associated with a 5-year mortality rate equal to or greater than the mortality rate of individuals with prostate or breast cancer (Margolis, et. al., 2011).

There are few clinical treatments for DFUs and other diabetic wounds. This unmet clinical need is only expected to grow. Because of the range of factors that contribute to DFUs, these wounds are difficult to treat. Current treatment options for DFUs include tissue removal, negative pressure therapy, and topical applications (Margolis, et. al., 2011) (Pop & Almquist, 2017). However, these therapies are still ineffective for a substantial fraction of the patient population. Ultimately, they do not promote a healthy environment for tissue regeneration, rather they only attempt to alleviate the side effects of diabetes and DFUs (Pop & Almquist, 2017).

MAP gel provides a microporous and controllable porosity structure as well as a degradable wound healing environment that promotes cellular network formation, including cell-cell adhesion and cell-extracellular matrix adhesion and signaling, and vascularization, or formation of blood vessels (Griffin & Weaver, 2015). The clinical goal of MAP gel is a one-time injection applied topically to a wound and upon annealing, or hardening, of the gel, healing times and health of the tissue would improve (Griffin & Weaver, 2015). MAP gel has already proven to be a more successful alternative to standard poreless hydrogels as it reduced the wound area remaining after

5 days from 100% for standard hydrogels to 60% when injected into the wounds of hairless (CLR:SKH1-*Hr$_{hr}$)* mice (Griffin & Weaver, 2015). In addition, it has also demonstrated two other key improvements, including decreased inflammation and increased integration with healthy tissue. Therefore, the aim of this proposed project is to continue to build upon the success that MAP gel has already proven in order to continue to advance the best possible solution to the unmet clinical need of diabetic wound healing.

The overarching goal of our project is to develop a MAP-EGF formulation that can be applied in a murine wound healing model, that will improve chronic wound healing through enhanced regeneration with MAP hydrogel. MAP gels improve wound healing by promoting a pro-healing microenvironment, or an environment containing the necessary signaling molecules that will recruit cells to restore healthy tissue and are present in a healthy healing environment (Rice et. al., 2012). In conjunction with the Griffin lab, it has been hypothesized that a chemotactic agent, such as epidermal growth factor (EGF), will accelerate tissue integration into the MAP hydrogel. EGF has been proven to enhance the healing of the epidermal regeneration of skin and thus was chosen (Brown, et. al., 1989). First, the concentration of EGF loaded into the MAP gel that will elicit a significant cellular response will be optimized using a cell migration assay, or test. Then, the loading and release of EGF from the MAP gel will be characterized using an enzyme-linked immunosorbent assay (ELISA), which is used to detect the presence of proteins to understand the amount of growth factor released into the wound site (ThermoFisher Scientific, n.d.). Finally, evaluating the effects of lyophilization, or removing water by sublimation, on the loading and release of EGF will indicate the feasibility of stably storing the MAP gel in a freeze-dried state. After optimization of these parameters, the formulation will be tested in an animal wound healing model.

Necessary supplies will be provided by the Griffin lab. The resources that will be deemed appropriate to use will be determined by Lauren Pruett, a PhD candidate in the Biomedical Engineering department and our immediate contact for our capstone project, in conjunction with Donald Griffin. This technical project is an example of a technology or treatment option that could be considered in the STS Research Paper's analysis of inclusive innovation because if this treatment was not available for those of lower income, including Medicare and Medicaid recipients, then there would be a clear disparity in quality of care for diabetic wound healing. In addition, because there would be a decision on whether to expand coverage of Medicare and Medicaid to encompass this treatment option, the framework for STS analysis of techno-politics would be applicable.

Analysis of Diabetic Care through a Techno-Political Lens

The *techno-political framework* and *inclusive innovation* will support the analysis of diabetic care, specifically MAP gel for wound healing applications that is addressed in the technical component. The main human and social dimension that is of issue is how politics in the United States, especially in relation to the coverage that Medicare and Medicaid offer, impact a diabetic patient's choices in treatment and quality of care (Kumar & Berlin, 1998). This can be analyzed through the research of the total number of different options for various treatment plans of diabetes, including blood sugar monitoring, insulin costs, medicines to lower A1C and blood sugar, and the treatment of side-effects, which wound healing would fall under. The total number of all possible options can then be compared to the total number of options that are covered under Medicare and Medicaid in order to understand the total percent coverage of diabetes treatment options for the elderly and those of lower income through Medicare and Medicaid. In addition, an

analysis of whether the best options are covered by Medicare and Medicaid will add to a complete understanding of whether healthcare politics affects a diabetic patient's quality of care.

The central stakeholders to this social and human issue are infinite but the ones most affected by the politics and technology of diabetic care are the patients themselves, individuals on Medicare and Medicaid, individuals on private insurance plans, doctors, hospital systems, the government, especially the agencies that have influence over healthcare policy, tax payers and families of patients. In the STS Research thesis, the framework of *techno-politics* will be used to understand each stakeholder's perspective on diabetic care and how politics, particularly those relating to healthcare coverage and healthcare policy, impact the relationships between these stakeholders. In addition, the technology component of techno-politics will be analyzed as how do policies typically develop around technologies in order to create order. The predictive technical case study that will be developed is on how policy may affect MAP gels and the treatment's availability to the public after it has been approved by the Food and Drug Administration (FDA).

In his article "Do Artifacts Have Politics?", Winner argues that technologies can be judged not only on how they succeed in generating efficiency and productivity, but also whether they generate power for good or for bad in society, thus resulting in politics (Winner, 1980). Therefore, through this *techno-political framework* that Winner has built, the object under analysis in this research project will be both diabetic care in its entirety as well as the aforementioned case study of MAP gel. It will be determined whether there are positive or negative power dynamics created through Medicare and Medicaid's coverage of specific treatments. In addition, power dynamics and political influence may arise if Medicare and Medicaid choose to cover treatments that are not of as high quality as other available options. The second part of the analysis via the *techno-political* framework is an understanding of how policies arise concerning a new biomedical technology,

such as MAP gel. In order to provide this predicative analysis, case studies similar to MAP gel will be looked at to understand the contributing factors to whether the treatment was covered by Medicare and Medicaid and how the government regulated the treatment.

In addition, in his book, Amadei describes that the appraisals of communities, or the inspection of a community in order to understand their daily struggles, can aid in the instruction of how communities can stand to improve their quality of life by leveraging their own talents and resources (Amadei, 2014). This book will be utilized to understand communities in which diabetes healthcare affects. The guidelines and methodology can be applied to communities, defined for this research as individual states, who experience higher rates of diabetes or poor quality of care to understand what factors in their state may be encouraging these trends. This will demonstrate whether they are predisposed to have higher rates of diabetes due to the quality of their life and availability of healthcare. The analysis of the diabetic care landscape through Amadei's description of the appraisals of communities supports a definition of inclusive innovation because if the availability of diabetic care treatments, such as MAP gel, is not decided with these communities and their inherent strengths and struggles in mind then it is not inclusive innovation.

To support the STS framework of responsible innovation will be the key arguments that Wiebe E. Bijker offers in his article. He states that the focus of technological culture used to be how to study it, but now it has become how to build the culture around technology (Bijker, 2017). The argument that will be critical to this analysis is when Bijker states is that we must invest in the future of technology. This is not to say we must spend more money developing technologies themselves, but rather investing in preliminary research on how they will affect society. Bijker urges us to invest in constructing technological worlds rather than allow them to passively develop (Bijker, 2017).

In the STS research paper, these arguments will be utilized by drawing a connection between Bijker's argument and how we must plan in advance for new and emerging healthcare technologies in order to carry out responsible innovation. I will utilize it in order to make a connection to my technical report in describing that before a technology like MAP gel is available in the clinic, the implications of its use and availability to all groups of people, including lower income patients, for diabetic wound healing must be considered.

Research Question and Methods

The question that will be addressed is: How does financial insecurity affect an individual's quality of care and treatment options for patients of lower income who suffer from diabetes in the United States of America? As previously addressed in the introduction, this question is extremely relevant as there is expected to be an 83% rise in the number of patients who suffer from diabetes and a majority of these patients are impoverished (Margolis, et. al., 2011). Ensuring that all patients receive adequate and equal treatments of their disease, especially in the United States, is critical in order to continue to respect each citizen's human dignity and right to life. Thus, it can be argued that the country's respect for its lower income citizens and elderly is directly related to the quality of care and equitable distribution of healthcare that it provides.

There will be two central methods of evidence collection that will be employed in order to understand and draw a conclusion on the research question to be addressed. The first method collection will be to use surveys and primary data, specifically the data that the American Diabetes Association, the Centers for Disease Control and Prevention through the U.S. Department of Health & Human Services and the Agency for Healthcare Research and Quality have gathered and delve into whether there are associations between quality of care, available treatment options and the income level of a diabetes patient through traditional data analysis. For instance, I will use the

Diabetes State Burden Toolkit through the U.S. Department of Health & Human Services in order to analyze the cost of diabetes in historically poorer states as compared to historically wealthy states in order to know whether there is a disproportionate relationship. This is an important method because it gives a national scope of the care of diabetes and how well medicine in the United States is serving all of its patients of different backgrounds and income brackets that suffer from diabetes. In addition, techno-politics informs the analysis of the whether there are power dynamics created through the coverage of Medicare and Medicaid because the total percentage of these treatments that these insurance plans cover will allow for the deduction of whether there is equality amongst different income levels..

As the central purpose of the STS Research paper is to draw connections to the human and social dimensions of a technical project, the second method of data collection will address inclusive innovation by interviewing advocacy groups in Washington, D.C., including the American Diabetes Association of Greater Washington and the Diabetes Advocacy Alliance, on their perspectives on disparities in quality of care of diabetic patients (Novo Nordisk, 2019). This will add a humanistic dimension that is critical in order to ensure respect for people runs rampant through the Medicare and Medicaid healthcare plans. If patients do not feel as though Medicare and Medicaid fully covers their diabetic care needs, then this is an alarming sign that the systems have not been designed to accurately meet the inclusive innovation requirements. Incorporating a dimension like this is important for future advocacy purposes in order to emphasize the importance of creating change in this sphere of quality of care disparities. An Expected Timetable (Table 1 in the Appendix) lays out the plan for my Technical Project and STS Project Deliverable over the rest of this year and second semester.

Conclusion

The deliverable of the technical project will be a report on the optimized MAP-EGF formulation, which will be used by the Griffin lab and others to further their research in translation to clinical applications. The impact that this project will deliver, if successful, is a better understanding of how growth factors can be optimized with MAP gel to target the healing of other tissues. The central problem behind the STS Research Paper is whether financial insecurity is the driving force behind the disparities of quality of care of diabetes. The framework of techno-politics will structure an analysis of Medicare and Medicaid's diabetes coverage. The goal of this research is an understanding of whether there are less treatment options than private insurance. Conclusions will be drawn through analysis of the data collected from governmental agencies of the profile of diabetic healthcare across the country as well as focused interviews with advocacy groups, who hold an important perspective on how quality of care affects an individual's or family's life. This research has the potential to support advocacy groups' missions of equalizing and improving quality of care for those of whom it is often out of financial reach. If society is able to properly respond to research such as exposure to differences in quality of care for diabetic patients, governmental policy could be implemented to ensure equality for all citizens and an increase in empathy from caregivers whilst treating their patients.

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Appendix

Table 1: Expected Timetable for Technical and STS Research Projects		
Date	Technical Project Deliverable	STS Project Deliverable
End of November and Semester	• Capstone Proposal, including preliminary results and detailed plan for how Specific Aims of the project will be achieved and when second semester • Elevator pitch on the project • Fall Progress Project Update, including feedback from advisor on quality of work and Proposal report • 1 to 2 more studies in order to achieve our specific aim: Optimize the concentration of EGF loaded into MAP gel using a cell migration assay to achieve the most efficient concentration of EGF that promotes a cell response	• Peer and advisor review of prospectus. • Reevaluation and confirmation of direction for STS thesis after receiving reviews of Prospectus • Prospectus Presentation • Prospectus Reflection
End of January	• Carry out second specific aim: Characterize the loading and release of EGF from MAP gel using an ELISA to better understand the quantity of EGF retained by the gel. • Progress report update for technical advisor. • Analysis of studies and data and complete section of report on this aim.	• Finish introduction, problem statement, research question and background research. • Complete a timeline of research that will be done throughout the semester.

End of February	• Carry out third specific aim: Determine the effects of lyophilization of MAP on protein loading. • Progress report for technical advisor. • Analysis of studies and data and complete section of report on this aim.	• Conduct interviews with advocacy groups. • Complete data collection through U.S. governmental agencies. • Complete analysis of the issue under the STS framework of techno-politics. • Finish all STS research components.
End of March	• Test MAP-EGF formulation that was optimized in a murine model to understand its in vitro application and results. • Progress report for technical advisor. • Analysis of studies and data and complete section of report on this aim.	• Finish (most of) technical component portion of the thesis. Anything that will be added will be of findings after this central body of the paper was written.
End of April and Graduation	• Complete report and analysis to define the optimal MAP-EGF formulation that we have determined. • Report out on findings through final Capstone presentations.	• Review of STS and Technical Thesis with technical advisor, STS advisor and through peer feedback. • Complete thesis.