Interrogating the Cellular Impact of Sonodynamic Therapy on Glioma Cells

Evaluating Cancer Care Insufficiencies in the United States Healthcare System

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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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Introduction - Problems in Cancer Care

Cancer care in the United States often fails to provide equitable outcomes among different socioeconomic and ethnic groups. The complex nature of oncological medicine and the interface of patients with a wide array of medical professionals and specialists ultimately occlude information from patients. Lack of transparency and discussion of cost-value treatments leads to significant financial hardship for patients, taking a toll more prevalently on low-income and patients of ethnic minority groups (National Cancer Institute, 2024). Combined with the lack of alternative options, this leads to poor patient autonomy. Financial motivations also play a significant role in treatment recommendation plans for patients.

This problem is only expected to expand, as the number of cancer patients is expected to rise appreciably in the United States as a significant at-risk demographic of people above 65 years old is expected to double by 2030 (Hansen, 2024). My STS research will focus on a comparative analysis of various healthcare systems to interrogate the underlying factors driving positive and negative patient outcomes. Utilizing the multi-level perspective (MLP) theoretical framework, I will analyze peer-reviewed literature that both quantitatively and qualitatively describes patient and physician experiences in different countries. I will also include an analysis of legislation introduced by various countries that directly relates to the accessibility and success of their healthcare systems, potentially establishing a connection between prevailing laws and cancer patient experiences.

The goal of my research is to identify specific changes that the United States can implement to improve cancer patient outcomes. In conjunction with this discussion, the technical paper will present an example of recent emerging innovations in cancer treatment, and how novel treatment methods have the potential to limit patient costs and harmful side effects. The connection between these two papers will propose actionable insights for improving cancer care outcomes and equity through both systemic and technological approaches.

Technical Report - Interrogating the Cellular Impact of Sonodynamic Therapy on Glioma Cells

The technical research report, *Interrogating the Cellular Impact of Sonodynamic Therapy on Glioma Cells,* will specifically examine a novel treatment method for Glioblastoma Multiforme (GBM). This form of brain cancer is among the most fatal and prevalent types, accounting for 50.1% of all brain tumors, and with a 5-year survival rate of just 6.9% (National Brain Tumor Society, 2024). Currently, the leading clinical measure taken for the treatment of GBM is surgical removal. This method is highly invasive, expensive, traumatic, and still does not result in a long-term cure. In the search for new therapies to treat these tumors, a novel therapy was created called sonodynamic therapy (SDT). Initially used to treat skin cancer, SDT utilizes focused ultrasound (FUS) and a *sono*sensitive drug (Marcus and de Souza, 2024). Rather than using ultrasound as a diagnostic tool as in cases of pregnancy, a lower-frequency ultrasound can have therapeutic effects. In the case of SDT, patients orally take the sonosensitize drug which is absorbed specifically by the tumor cells. Then, FUS is aimed at the tumor, and the acoustic nature of the ultrasound waves causes the cancer cells to vibrate back and forth, ultimately causing them to rupture. This therapy selectively kills glioma cells in a completely non-invasive, non-ionizing manner, and is currently in clinical trials. Our project will be advised by Natasha Sheybani, a professor in the Biomedical Engineering department at UVA.

Planned Research Methods

Martins (2021) argues that the existing literature surrounding this treatment is often lacking in its description of FUS parameters, a crucial element in determining the effectivity and replicability of SDT. This argument supports my own investigation into the literature, and helped form the basis for my technical project. These parameters include the power, voltage, and time period of the ultrasound. It is quite easy to change these parameters, but it is unknown exactly what will result in different parameter settings. This project will employ the use of a mouse cell line for *in vitro* experiments to establish a procedure for optimizing the parameters.

Secondly, this project will investigate secreted cells from the mouse cells under SDT conditions. Our preliminary work has shown that extracellular vesicles (EVs) are secreted by the tumor cells during treatment. These EVs are crucial cell signaling molecules that carry proteins, nucleic acids, and other mechanisms of signaling that could be implicated in further cancer development. By isolating these EVs and running various protein assays, we can characterize them and determine what roles they may be playing in the growth or inhibition of GBM. Furthermore, this project will involve the creation of a novel structural support system to help control FUS transducer placement within the experimental setup, to minimize displacement and increase the ease of replication by removing human error-inducing factors of hand placement and visual inspection.

STS Report- Evaluating Cancer Care Insufficiencies in the United States Healthcare System

The healthcare system in the United States is often confusing to navigate and can serve to hinder successful patient outcomes. The anguish experienced by cancer patients is often amplified by their perceived lack of autonomy and financial stress. Furthermore, these experiences are exacerbated among patients of minority groups. It is important to identify missteps within our current standards of care for cancer patients such that specific actions can be undertaken to amend them. The underlying question my research will address is how the United States can modify its healthcare system to promote positive patient outcomes among cancer patients.

Many peer-reviewed, published studies have focused on analyzing a variety of negative outcomes and shortcomings in cancer care, providing evidence to support the idea that this is indeed a prevailing issue in the United States. One aspect of insufficiency in cancer care that has been identified is a pattern of miscommunication between patients and their physicians. For example, a study of terminally ill patients found that it was communicated to them that they would have a median survival of 90 days, while physicians estimated that survival would be just 75 days, whereas, in reality, the actual median survival was just 26 days (Lamont, 2001). A separate peer reviewed study on colorectal cancer patients found that 81% “did not understand that chemotherapy was not at all likely to cure their cancer” (Weeks, 2012, p. 1713).

Furthermore, this lack of adequate communication and understanding is exacerbated among patients with lower education or English fluency. This discrepancy is often not resolved even with the use of translators, as a peer-reviewed study found an average of 31 errors per encounter between physician-translator-patient arrangements (Hansen, 2012). The propagation of these mistakes results in non-US-born patients being less likely to receive recommended therapies, and less likely to report excellent care (Hansen, 2012). These sources provide candid and surprising statistics directly from patients and physicians alike, showcasing how stark the contrast can be among their respective knowledge and control over the situation.

Patients are not usually provided with comprehensive financial analysis for their care, resulting in financial toxicity. Previous studies have observed 71% of patients reporting financial hardship within a year of their diagnosis (Winstead, 2022). Financial hardship has also been found to disproportionately affect patients of racial minority groups (National Cancer Institute, 2024). Much of these financial problems stem from the prevailing mainstream protocols followed by physicians, among whom have admitted that they have “no motivation to consider the cost to the system”, that they are “encouraged to prescribe expensive treatments”, and that “we lack studies that show the best practices and values for patients” (National Cancer Policy Forum, 2013, p. 16-17). Physicians have also reported difficulty in candidly explaining to patients the impending fatality of their situation, not wanting to inflict distress.

Research Methods

To perform my STS research, I will conduct a literature review of peer-reviewed papers published in reliable and trustworthy journals. Through this search I will include both quantitative and qualitative evidence regarding the interplay between patients, physicians, and insurance providers. Direct quotations of the experiences from these member groups will present specific examples of sentiment, while statistical data aggregated from published studies will encapsulate larger trends. Furthermore, I will comparatively analyze the healthcare systems of various countries with differing payment protocols. This will entail research into political and legislative impacts on healthcare and its relation to cancer patient outcomes.

I will analyze evidence using the MLP theoretical framework, considering the perspectives of patients, physicians, medical regulatory bodies, insurance providers, and their subsequent motivating factors. The broadest layer of the MLP framework, the landscape, can be described by overarching societal shifts in cancer care, with a push for equitable access to treatments. This level sets the context within which all other activities occur, shaping the norms around patient autonomy and the imperative to alleviate financial toxicity. The regime level involves the current mainstream practices and norms within the current cancer care structure as instituted and upheld by regulatory bodies and insurance and big pharma companies. This regime often prioritizes expensive treatment approaches and fosters an environment that does not fully prioritize transparent communication. This niche level is where innovative ideas and new approaches to cancer care are discussed and attempted to be implemented. This level includes novel cancer treatment methods like SDT, and new policy ideas to offer better and cheaper cancer care. Integrating the MLP framework provides a multi-dimensional understanding of the barriers to effective cancer care.

Conclusion

The combined portfolio of papers in this eventual thesis will discuss technically the implementation of a custom-designed, 3D-printed structure to augment the experimental replicability of a preclinical *in vitro* study of SDT, as well as a methodology for more general FUS parameter optimization. This represents a novel innovative cancer treatment method that is non-invasive and less physically taxing as the prevailing glioblastoma clinical care. The STS paper will analyze the detriments of modern cancer care through the lens of the MLP framework, and present potential solutions to the problems of poorly informed patients, financial motivations in treatment, and lack of societal and employer support for patients and their familial caretakers. These ideas will be introduced and supported by evidence of success in other countries and systems in hopes of inspiring further research into changing the standards of cancer care in the United States.

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