Designing Ultrasound Image Analysis Techniques For Dc101-Treated Tumors In Mice
(Technical Paper)

Effect Of Socioeconomic Background On Breast Cancer Mortality Rates
(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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Prospectus

Breast cancer is the second leading cause of cancer-related deaths in women with over 43,000 estimated deaths for 2022, and is also the second most common cancer in women, making up 15% of all new cancer cases (National Cancer Institute, n.d.). Chemotherapy is a form of treatment that can be provided preceding tumor removal surgery as a method of reducing the size of the tumor by either killing cells that proliferate rapidly or preventing them from proliferating (National Cancer Institute, 2022). The chemotherapeutic drugs are ingested or injected and then travel through the blood and access the tumor through the tumor’s vasculature, its system of blood vessels. A method being developed to increase the effectiveness of chemotherapy is using an anti-angiogenic drug which will help normalize the irregularities that are commonly found in the blood vessels of tumors, which are caused by the unregulated blood vessel growth characteristic of cancer cells (Jain, 2005). Normalizing the tumor vasculature will open the blood vessels to make transport of drugs through the blood more effective, while also decreasing the chances for the cancer to metastasize, or break away and spread to a new location in the body.

The technical project and tightly coupled STS research project being proposed will address the high mortality rate from breast cancer. The objective of the technical design project is to create an image analysis program that would work through an existing ultrasound machine, is coded using MATLAB, and would output statistics relating to the blood flow in the tumor as well as what percentage of the tumor is accessible through the blood vessels. By doing so, breast cancer researchers will be better able to collect data of the effects that different drugs have on tumor blood vessels. The development of this treatment would help decrease the required chemotherapy dosage needed for the treatment to be effective, while also decreasing the duration of treatment. This would make cancer treatment more accessible to women from lower income groups, who have been found to have higher mortality rates when compared to higher income groups (Nattinger et al., 2017).

DESIGNING ULTRASOUND IMAGE ANALYSIS TECHNIQUES FOR DC101-TREATED TUMORS IN MICE

The image analysis program will read a series of tumor cross-sectional images over time in order to track the progression of microbubbles through the tumor vasculature. Microbubbles are composed of a gas that is contained inside of a protein, lipid, or polymer shell (Sirsi & Borden, 2009). Because microbubbles are highly responsive to ultrasound, they can be used for imaging, as well as drug and gene delivery. Figure 1 shows a side-by-side comparison of standard ultrasound imaging with contrast-enhanced images. Contrast-enhanced ultrasound is an imaging technique that allows for the microbubbles to appear as a bright signal under ultrasound which makes it effective for tracking the tumor's vasculature when injected into the local bloodstream (Ellegala et al., 2003). The microbubbles are coated in a molecule that is targeted to α-integrins, which are receptor proteins that are involved in the process of forming new blood vessels, such that they adhere to the endothelial cells of the tumor's blood vessels. This allows for the use of ultrasound to produce an image of the structure of blood vessels since the microbubble signaling will remain localized to the tumor vasculature.

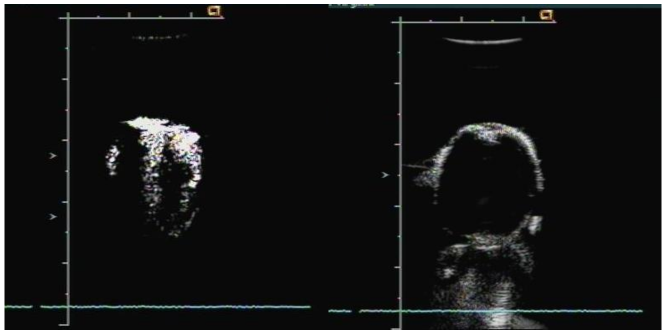

Figure 1: Ultrasound Images of DC101 Treated Tumors. The left image was taken while performing contrast-enhanced ultrasound to show the tumor’s vasculature, and the image to the right is a standard ultrasound image that shows the size and shape of the tumor (Villarroel, 2022.

This technique for imaging is useful for the technical project because of how it is directly applicable to the field of research in anti-angiogenic drug-based cancer treatment. Angiogenesis is the formation of new blood vessels, and is a process that tends to occur uncontrollably inside of tumors, where cell proliferation is unregulated by the body. As a result of this unregulated vessel growth, tumor vasculature tends to develop abnormally such that blood vessels are dilated, tortuous, and leaky. Abnormal vasculature can hinder the effectiveness of most of the common treatments available for cancer, including chemotherapy and radiation therapy, by decreasing blood flow and making it more difficult for drugs to reach their target locations. This technical project focuses on improving drug delivery, so the focus is primarily on the impact it has on chemotherapeutic drugs since they travel through the blood and are impacted by the reduced blood flow and leaky vessels found in tumors (National Cancer Institute, 2022).

A method developed to address the problem caused by these abnormalities is the use of anti-angiogenic drugs that inhibit the unregulated growth of the blood vessels and make the vasculature less dilated and leaky, a process called normalization which results in an increase in blood flow with the right dosage (Jain, 2005). Vasculature normalization can improve drug delivery to the tumor, making chemotherapy more efficient and thus requiring lower dosages for similar effectiveness. This is significant because lower chemotherapeutic drug dosages will result in less side effects for the patients, potentially decreasing mortality rate as well as the recovery period. The data that will be collected for the technical project comes from mice with breast cancer tumors that have been treated with the anti-angiogenic drug DC101, along with an untreated control.

DC101 inhibits angiogenesis specifically by targeting vascular endothelial growth factor 2 receptors, which are receptors in the pathway responsible for endothelial cell growth, migration, and survival, as well as regulating blood vessel permeability (Hicklin & Ellis, 2005). The effects of DC101 on breast cancer tumor vasculature will be viewed through the use of contrast-enhanced ultrasound to allow for visualization of the blood vessels over the course of treatment as well as between the two sample groups. This will allow for data analysis of the effects that DC101 has on the tumor's vasculature by showing how quickly drugs could theoretically enter the tumor as well as how much of the tumor they would be able to access. Images taken over time can be used to calculate the rate of drug flow through the vasculature using the microbubbles as a model drug, and images taken after full perfusion of microbubbles will show the full range of accessible vasculature in the tumor.

The motivation for developing this program is that there is no current method to track in real time the progression of microbubbles in a tumor or for modeling the vasculature of a normalized tumor. The program would assist researchers that are developing treatments that involve anti-angiogenic drugs by providing concrete data on the effects that a treatment had on the structure of the tumor vasculature as well as on drug delivery. This will make it easier for them to adjust their treatment plan after each trial, such as modifying the dosage of the anti-angiogenic drug. Under the advisement of Richard Price, the fall semester will be used to develop the program for analyzing time-lapse images of tumors at different cross-sections. The spring semester will be used to develop a program that can generate a three-dimensional model of the tumor vasculature in AutoCAD using the various tumor images.

SOCIOECONOMIC BACKGROUND ON BREAST CANCER MORTALITY RATES

The STS topic will focus on how varying socioeconomic backgrounds affect the mortality rates in breast cancer patients. Data will be collected on the differences in how early the cancer is diagnosed, the rate of survival once diagnosed, and the overall mortality rate of breast cancer, comparing across different socioeconomic groups (SEG). This topic is significant because of how deadly breast cancer can be, as evident by its high mortality rate among women compared to other types of cancer as the second most common cancer-related cause of death (National Cancer Institute, n.d.). To ensure that all patients are receiving the quality of care necessary to enable recovery, analysis will be conducted to determine to what extent cost and accessibility has an impact on an individual's chance to survive breast cancer.

Across the three metrics of mortality rate, case fatality, and incidence rate, Lundqvist et al. found that individuals that were classified as having a background of a lower SEG had higher mortality rates and case fatalities, whereas higher SEGs had higher incidence rates (2016). The higher mortality and case fatality could be due to either inaccessibility to more expensive and effective treatments or other lifestyle choices that impact health that are outside of the standard treatment procedures. An example of differing access to certain treatments is that higher SEGs were found to be more likely to have radiation therapy following breast conserving surgery, which would be more expensive a procedure.

However, even when controlling for treatment factors, women in higher SEGs had lower case fatality rates, indicating that there are factors outside of the treatments provided that have a significant impact on an individual's chances of survival. In support of this, a study by Binkley et al. that investigated the side effects associated with chemotherapy found that physical rehabilitation during or after treatment can increase a patient's chances of survival (2012). They also found that few women are referred to, or informed about the benefits of, rehabilitation. Further study into how different SEGs participate or are informed about rehabilitation is necessary to determine if this is a method of improving survival rates for all patients.

By analyzing the disparities that exist between the different SEGs, as well as consulting the members of those same groups, more effective treatments or policies could be enacted to decrease the mortality and case fatality rates for those disproportionately affected. Using the Social Construction of Technology framework, treating members of lower and higher SEGs, as well as medical experts, as social groups that are consulted can help enact reforms that are both effective as well as acceptable (Bjiker, Bonig, & Van Oost, 1995). The discourse that occurs between the engineers and designers and the social groups can improve how informed patients of all SEGs are, while guiding designers towards research or development that would result in the highest increase in survivability.

CONCLUSION

The technical project aims to improve the efficiency of cancer treatment research so that future treatments can be more effective and affordable by providing a tool that can efficiently present the results of their trials and informing them on how to adjust future trials. The STS research topic seeks to decrease the disparity between different socioeconomic groups by targeting policies or accessibility to treatments. This makes the STS topic tightly coupled to the technical topic, since the results of the technical design project could reduce the overall cost and duration of cancer treatments, making the process more affordable and accessible for a wider range of socioeconomic groups. Similarly, results of discourse between designers and the patient or medical expert social groups could help inform the course of research or application of the technical project.

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