

A Therapeutic Screening Software for Vessel Normalization in Melanoma
(Technical Paper)

**An Actor – Network Theory Analysis of the Impact of Artificial Intelligence on Healthcare
and Humanity**
(STS Paper)

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On my honor as a University Student, I have neither given nor received
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Introduction

The human-computer hybrid, a medical and technological phenomenon that has yet come to fruition, may become a reality within the next several decades. Technology is the most ubiquitous it has ever been in healthcare, exhibited by its use in diagnostics, treatment, record-keeping, data-analysis, and innumerable other functions (Mamlin & Tierney, 2016). The need for technological innovation to improve the efficiency of healthcare and the personalized, compassionate care from human beings is a critical balance to maintain. Furthermore, there has been an increased use of artificial intelligence (AI) in medical research and medical practice (Hamet & Tremblay, 2017). Governmental regulations have not caught up with the rapid progression of AI, which demands a discussion on the repercussions of AI in healthcare. Humanity is an important value to society and should especially be carried into the field of medicine. Technological innovation should be designed to improve healthcare, but not at the expense of societal values. The proposed STS research paper will analyze the positive and negative upshots of AI on healthcare and humanity and deliberate potential future directions regarding AI.

Although the evolution of AI in healthcare must be examined more thoroughly, there is no question that technology is essential for the growth of improved medical treatment. Cancer poses an eminent threat and has consistently been one of the leading causes of death for decades (Siegel et al., 2019). Doctors use various different avenues of cancer treatment to reduce symptoms, eliminate tumors, and prevent recurrence. However, the consistent high rates of mortality associated with cancer demand further development of treatment and analytic methods, particularly involving technology. As such, technical research will be conducted on the

development of an optimized therapeutic tumor vessel screening software that will improve the analysis of a novel cancer therapeutic.

Technical Topic

The human body is an incredibly complex system, which presents a challenge in investigating pathological conditions such as cancer. Cancer is one of the leading causes of death in the United States with approximately two million new diagnoses and 600,000 associated deaths each year (Cancer Statistics - National Cancer Institute, 2015). In particular, there are about 100,000 diagnoses and 7,000 deaths each year due to melanoma, a form of skin cancer (Melanoma Skin Cancer Statistics, n.d.). Cancer treatments target cancerous cells and related pathways to halt cancer progression. One such pathway involves the coexistence of cancer cells with the surrounding blood and lymphatic vessel network. The generation and maintenance of this vascular network, known as angiogenesis, is essential for tumor growth and favors the spread of cancer, or cancer metastasis. The vessels promote this growth and spread by compensating for the tumor's high oxygen and nutrient demand (Folkman, 2010). Also, the cancer cells secrete high levels of pro-angiogenic factors, which contribute to the creation of a disordered vascular network characterized by immature and permeable blood vessels. The abnormal vascular network then further limits the subsequent immune response, as vessels are one factor that modulate T-cell, a type of immune cell, trafficking (Viallard & Larrivé, 2017).

As such, tumor blood vessels are a key target for cancer therapeutic management, as antiangiogenic therapies can normalize tumor vasculature to ultimately restore immune function. Many current therapeutics target a pro-angiogenic factor named vascular endothelial growth factor, or VEGF (Melincovici et al., 2018). These current cancer therapeutics have demonstrated effective results, but often yield temporary remission as the possibility of recurrence following

treatment is highly likely with most cancers. Therefore, additional pathways that lead to vessel growth are crucial in effectively targeting the vascular network. Previous studies have identified a protein called hornerin, which is located on cells that line blood vessels and is independent of VEGF. Hornerin is part of a compensatory pathway in angiogenesis. Hornerin knockdown using silencing RNA (siRNA) results in a reduction of protein expression, allowing researchers to study the impact on the tumor environment. In studies concerning pancreatic cancer, hornerin knockdown resulted in normalization of the vessels and reduced tumor burden (Gutknecht et al., 2017). Additionally, hornerin is expressed in psoriatic and wounded skin, elucidating its potential in melanoma treatment (Takaishi et al., 2005).

For analysis of therapeutics, such as those that result in hornerin knockdown, comparing the characteristics of tumor vasculature to normal vasculature can provide an understanding of drug efficacy. The Rapid Analysis Vessel Element (RAVE) software is a vessel analysis software that was introduced almost a decade ago (Seaman et al., 2011). RAVE performs analysis of vascular environment images with few variations. An image is uploaded to the software, which performs several operations to compile and output vessel parameters such as vessel volume fraction, vessel length density, vessel radius, and fractal dimension. Although operational, RAVE only has the ability to analyze one image at a time, limiting the efficacy of large-scale analysis due to the time-consuming nature of the program. Additionally, the software lacks a single data output function, as well as the capacity to copy and paste. Therefore, by the end of the academic year, the capstone team will deliver an optimized RAVE software. The deliverable will include characteristics such as batch processing and a more user-friendly output, including a single, exportable file containing all the vessel parameter data. Further, the technical research project will upgrade the existing RAVE software by incorporating an algorithm to

automatically set appropriate thresholds for individual images. This algorithm will reduce the processing time for multiple images and reduce potential variations produced by manual threshold entry.

The proposed research project will offer an optimized therapeutic screening software that presents an effective way to screen new therapeutics directly targeting the tumor vasculature. The software will specifically be used to test the effect of a hornerin targeting therapeutic in melanoma; however, it has the potential to serve as a tool for vascular network analysis in a wide range of cancers.

STS Topic

Background

Countless scholars and innovators assert that artificial intelligence is the future and will transform the world as we know it (Talty, 2018). Artificial intelligence (AI) gives machines the ability to simulate capabilities of the human mind (Hamet & Tremblay, 2017). Often, AI is implemented to perform complex tasks with limited human intervention. In medicine, there are two primary areas of AI application: virtual and physical. The virtual branch makes use of machine learning, in which learned algorithms are applied to improve functionality of a machine as it proceeds to complete more tasks (Hamet & Tremblay, 2017). Applications of machine learning in medicine include computational genetic research and electronic health records. Contrarily, the physical branch of AI includes medical devices, robots, and other physical objects that play a given role in medical care (Hamet & Tremblay, 2017). Examples of physical implementations of AI in medicine include surgical robots, guided drug delivery, and brain-computer interfaces.

The primary application of AI in healthcare that will be explored in this proposed research paper is neurotechnology designed by Elon Musk's company Neuralink. Musk is developing a chip, called the "Link" to be implanted in the brain. Link interprets brain signals and possesses the ability to communicate with external technological devices solely using one's thoughts (Musk & Neuralink, 2019). Essentially, this development forms a "cloud" between a human brain and technology. Another goal of Neuralink is enhancement of human cognition by increasing the number and strength of active neurons firing in any given situation (Musk & Neuralink, 2019). The technology is being developed with higher biocompatibility, flexibility, specificity, and bandwidth than current technologies, to be utilized in various novel applications. Potential medical uses include seizure detection, prevention and treatment of neurodegenerative diseases, and allowing for sensation in and optimization of prosthetics (Pisarchik et al., 2019). Musk has mentioned that he strives to achieve a "symbiosis with artificial intelligence" and human beings (Neuralink Launch Event, 2019). Although the possibility of vast clinical benefits is appealing, there are several reasons to be hesitant about the further development of Neuralink. Specifically, there are ethical concerns regarding human enhancement including underdeveloped regulation on such unconventional technologies, unintended consequences of the device, transparency if using the device, privacy violations, a potential black market for selling data, and a possible threat to free will (Dadia & Greenbaum, 2019).

A technology with the power to merge humans and artificial intelligence incites a conversation about the potential ethical repercussions. Ethical priorities must be considered in regard to advanced neurotechnologies in a culture specific context, while still taking universal rights and global guidelines into account. The four main ethical priorities are privacy and consent, agency and identity, augmentation, and bias (Yuste et al., 2017). Pertaining to agency, it

is important to examine the impact of potential integration of humans and AI. There is a distinction between a human being, a person, and the self. For the purpose of this research, the “self” will not be discussed as its complexity distracts from the central thesis of the paper. The term ‘human being’ describes a member of the genus and species *Homo sapiens* based on biological characteristics. On the contrary, the term ‘person’ describes a being with sentience, reflective self-awareness, linguistic capabilities, and moral agency (Concept of Personhood - MU School of Medicine, n.d.). Personhood is associated with human beings through the concept of humanity. Though personhood has been demonstrated with other animals, humanity is the collection of characteristics that makes human beings distinct (Johnson & Cureton, 2019). An essential component of humanity is the ability to possess and uphold values as individuals and as a society. For this STS research, the value set will consist of the following: autonomy, personal freedom, mental integrity, privacy, and safety. Human rights, in both a philosophical and legislative sense, reflect these individual and social values (Ienca & Andorno, 2017). Neuralink possesses the ability to threaten the aforementioned value set, indicating the need for policy and regulation regarding the advancement of such neurotechnologies.

STS Framework

Actor-network theory (ANT) will be used to analyze this research problem. ANT considers the shifting relationships between natural and social worlds. The connections are between human and non-human actors with the ability to perform a given action (Booth et al., 2016). The actors are involved in integrated, but often unspecified, associations called networks that are not affected by external factors (Booth et al., 2016). A key component of ANT that contributes to the ambiguous nature of networks is a black box, which is a substitution for a complex system that is usually compressed due to its established and stable state (Miettinen,

1999). Transformation is the process in which one actor gives another actor a particular role to perform (Booth et al., 2016). The languages of the network and mechanism through which actors communicate with each other and initiate transformation are called intermediaries (K. M. Cresswell et al., 2010).

Critics claim that ANT remains superficial in description and does not possess predictive or explanatory power (K. Cresswell et al., 2011; Disassembling Actor-Network Theory - Dave Elder-Vass, 2015, n.d.). In response to this criticism, ANT scholars argue that the agency which characterizes an actor is separate from intentionality, which may further explain network processes. Other critics of this theory argue that application of ANT is inherently subjective when conveying the relative importance of actors due to the lack an out-of-network existence (Miettinen, 1999). Humans are seen as the dominant actors in many applications of ANT, which discounts the notion of reducing all actors to symmetrical entities. Additionally, certain professors claim that ANT does not consider pre-existing constructs, such as power dynamics, emotions, or rational thought, which limits the scope of critical understanding of any situation by failing to consider alternative peripheral elements (Whittle & Spicer, 2008). Regardless of these critiques, ANT provides a framework for investigating the dynamic between several sociotechnical interactions to better conceptualize the implications of human and non-human actors on each other.

ANT will be used to assess the influence of AI on society, medical care, and potential users of Neuralink. The actors include entities such as: AI technologies, Neuralink technologies, patients, researchers, and legislators. ANT will be useful in exploring the complexity of the networks connecting each actor, and the effects generated by technological implementations.

Research Questions and Methods

The research question this STS research paper will be exploring is as follows: can actor-network theory analysis on innovation of AI in medical care convey the significance and value of humanity enough to prevent it from being compromised for the sake of greater efficacy? In order to address the aforementioned question, documentary analysis, discourse analysis, and network analysis methods will be used.

Documentary analysis utilizes existing research and information to examine established areas of interest (Lawson, 2018). This approach will show recognized relationships between chosen actors. Articles from journals of healthcare communications, medical informatics, and medical humanities will be used as sources. The documentary analysis will provide evidence from related studies which will support the background information and initiate responses towards the posed research question. For example, the research article published by Elon Musk will be used, as well as review articles commenting on implications of Neuralink.

Discourse analysis is a method that studies language in use via inquiry within a sociocultural context (Yazdannik et al., 2017). Sources such as informational videos about Neuralink and literature reviews will be used to consider a more subjective response and further directions regarding the research question. For the discussion on ethical and moral ramifications, articles from journals of philosophy, editorials, and the Stanford Encyclopedia of Philosophy will be used.

Lastly, network analysis is a tool which assesses the abstract representations of a system composed of entities that are associated with each other and their dynamic influences (Contreras et al., 2019). This approach will be used to supplement the actor network theory analysis and provide insight into the nature of relationships between actors.

These methods will allow a comprehensive exploration of my research question by considering past research as well as allowing me to extrapolate towards future possibilities and the associated ethical consequences. The key words explored will be AI, humanity, and Neuralink. I have chosen these words because the study of all of them will point me towards the integrated network in which they are all connected and impact each other; therefore, helping me address the question that I proposed in a research paper set to be completed by the end of the academic year.

Conclusion

The technical component of this project will provide a new method of therapeutic tumor vessel screening via optimization of the RAVE software. The technical research project will also investigate the knockdown of the protein hornerin as an independent therapeutic agent against melanoma using RAVE in a technical paper. This approach will allow for more rapid and accurate analysis of tumor vessel images during cancer therapy trials. In addition, the software can be extrapolated and applied for tumor vessels of a multitude of cancers for more efficient testing and data reporting methods.

An STS research paper will analyze AI in medical research and healthcare and its impact on society to encourage continual evaluation of novel neurotechnologies. The research paper will also propose potential future impacts given the current trajectory of innovation. Lastly, the STS analysis will consider the need for prospective policy regulations of AI and innovative neurotechnologies in healthcare to emphasize the value in protecting humanity as the capacity of technology increases.

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