Volumetric Assessment of Pulmonary Artery Thrombus Burden
(Technical Project)

Analyzing the Medical Ethical Ramifications of Integrating Machine Learning into Patient Diagnostic Imaging Procedures
(STS Project)

A Thesis Prospectus
In STS 4500
Presented to
The Faculty of the
School of Engineering and Applied Science
University of Virginia
In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science in Biomedical Engineering

By
Nyota Patel

October 27, 2023

Technical Team Members: Rohey Colley and Yeongju Lee

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.

ADVISORS

Dr. MC Forelle, Department of Engineering and Society

Dr. Luke Wilkins, Department of Interventional Radiology

Dr. Kerstin Mueller, Siemens Healthineers

Introduction

Within the medical field, healthcare professionals often employ the use of imaging techniques such as computed tomographic (CT) and magnetic resonance imaging (MRI) to diagnose patients. However, the diagnostic decisions made by physicians are dependent upon the "rough estimates of outcomes" (Ricotta et al., 2008, p. 1059). Due to these estimates, healthcare professionals are prone to make diagnostic errors. These errors can arise either due to system-related factors such as poor communication and teamwork or cognitive errors. According to a study conducted by researchers at the John Hopkins University, approximately 40,500 patients die each year due to diagnostic errors (Dilsizian & Siegel, 2014). Addressing these errors through accurate and timely diagnosis is of crucial importance in reducing the number of deaths. Additionally, addressing this issue can lead to reduced health care expenses. Misdiagnosis often results in performing unnecessary tests and procedures, increasing health care expenses. Health care costs also increase by approximately $300,000 for every malpractice claim associated with misdiagnosis (Dilsizian & Siegel, 2014). Thus, it is of vital importance to reduce diagnostic errors in medicine not only to decrease death rates but also healthcare costs.

To reduce diagnostic errors, many hospitals have begun to use Artificial Intelligence (AI). AI is a branch of computer science that utilizes computers to imitate human behavior and thinking (Amisha et al., 2019). Within medicine, AI is being implemented to schedule appointments, digitize medical records, and contribute to surgical and medical treatments along with disease diagnostics (Amisha et al., 2019). Radiology is a branch of medicine that has embraced the use of AI. According to a study conducted in the radiology department of a cancer center, the use of AI in accordance with radiologists can help identify any abnormalities in

exams and detect negative exams with high accuracy while reducing the diagnostic time from several days to 1.0 hour (Topff et al., 2023).

Despite the benefits of AI, the use of AI to reduce diagnostic errors is part of a broader conversation regarding ethics and interdisciplinary collaboration. Successful integration of AI requires collaboration between various disciplines such as computer science, medicine, and the federal government. Additionally, regulators must take ethical issues such as concerns of data privacy into account to ensure safe and responsible use of AI in medicine. Therefore, it is important to take these factors into consideration before implementing the use of AI within diagnostic procedures.

For my technical project, my Capstone team and I will pre-process CT scans to identify regions of interest, and then we will develop and validate a machine learning (ML) algorithm that measures the volume of a clot that is blocking blood flow to the lungs. My technical project improves diagnostic accuracy by identifying the clot and ensuring a sufficient volume of the clot has been extracted from the patient. For my STS project, I will focus on how the implementation of ML algorithms into imaging diagnostics has impacted the medical community's ethical framework, known as the four pillars of medical ethics: autonomy, beneficence, nonmaleficence, and justice. Through extensive literature review, my STS project aims to understand how ML algorithms in diagnostic imaging impacts patient’s autonomy, beneficence care, and equitable distribution of resources in healthcare.

Technical Topic

Pulmonary embolism (PE) is a type of cardiovascular disease in which a blood clot, medically known as a thrombus, develops in the deep veins of your leg and travels up to the lungs, preventing blood flow in the pulmonary arteries. PE is one of the biggest causes of

morbidity, affecting 1-2 people for every 1,000 individuals annually in the United States (Wible et al., 2019). Thus, early detection, diagnosis, and treatment are key to reducing death rates. To diagnose PE, imaging methods such as CT are commonly used to identify the location of the clot. Current treatments such as anticoagulants (blood thinners) often increase the risk of bleeding in patients; thus, many healthcare professionals perform catheter-directed thrombectomy (Wible et al., 2019). This surgical procedure involves the use of a catheter that is introduced through the skin to mechanically remove the blood clots. To determine the efficacy of this surgical procedure, a retrospective study was performed in a single hospital with 46 PE patients over a 12-month period (Wible et al., 2019). All patients were treated with the FlowTriever device, a US Food and Drug (FDA) approved device that consists of a catheter system. The study concluded that when PE patients were treated with the FlowTriever device, the average mean pulmonary artery pressure improved, and all patients (100%) survived to hospital discharge (Wible et al., 2019).

Despite the surgical procedure's success in decreasing mortality, determining a sufficient clinical endpoint remains a complex challenge. When interventional radiologists (IR) perform a thrombectomy, it is difficult for them to estimate the amount of thrombus that is still present within the patient. To address this issue, my capstone team and I will develop and validate an automated method that accurately quantifies the volume of retrieved thrombus relative to the initial thrombus burden. To do this, we will first implement the use of picture archiving and communication system (PACS), which is a technology that allows for remote access to patient medical imaging data. Once we have obtained CT scans from PACS, we will export these images with a .dcm file extension to represent the Digital Imaging and Communications in Medicine (DICOM) file format. My team and I will then use Python's pydicom package to read

and modify the DICOM files. We will then develop a computational framework to perform automatic segmentation using machine learning, a subfield of AI focused on creating algorithms that can learn and make predictions from a dataset (Choy et al., 2018). To develop this framework, we will conduct literature review to identify existing algorithms that meet the following criteria: 1) accurately quantifies a lesion's physical characteristics, 2) programmed in Python, 3) short execution time of the program, and 4) high internal software quality. Algorithms that meet these criteria will then be modified by my team to create an ML algorithm, specifically a deep learning neural network algorithm (DLNN), a subset of ML. We will then use U-NET, which contains a DLNN architectural framework, to develop an algorithm that automatically segments our DICOM files to identify the PE. Segmentation plays a crucial role within the diagnostic process because it divides the images to isolate the regions of interest (ROIs). After performing segmentation, we will write additional code in Python to calculate the volume of the thrombus burden. To determine the efficacy and precision of our computational framework, we will compute the F1 score and the Dice coefficient, which are used to measure the accuracy and the quality of the segmentation process (Liu et al., 2022). Lastly, we will conduct a comparative analysis of the outputted volume of thrombus burden to that of the expected. The expected output will be obtained through collaboration with IRs, who will instruct us on how to perform manual annotations on the CT scans to determine the volume of the thrombus burden.

The proposed approach above for determining a clinical endpoint will drive advancements in the treatment of pulmonary embolism by providing characteristics of the clot that can be used as clinical indicators to improve treatment and management for patients diagnosed with PE. Additionally, our work can facilitate a clear diagnosis when patients return with symptoms due to recurrent PE. Lastly, the proposed method contributes to reducing

diagnostic errors by increasing accuracy and precision while reducing the diagnostic and surgical operating times as IRs are not required to manually annotate the CT scans.

STS Topic

Radiology is a medical discipline that often employs the use of machine learning to schedule and screen patients, process images, and automate the detection and interpretation of findings within medical images (Choy et al., 2018). According to various meta-analyses, ML algorithms have revealed a high accuracy, specificity, and sensitivity in diagnosing various illnesses such as cancer and COVID-19 (Cuocolo et al., 2020; Li et al., 2020). Therefore, the implementation of ML within diagnostic imaging processes can be a promising tool to increase accuracy and reduce system-related and cognitive diagnostic errors.

Although ML has shown success in patient diagnostic imaging procedures, ethical considerations need to be taken into account before adopting widespread use. The medical community has created its own set of ethical guidelines known as the four pillars of medical ethics. These four pillars emerged from the Hippocratic Oath, which originated in the 5th century B.C. (Veatch, 1997). In this Oath, physicians are required to uphold the highest ethical principles and to impose no harm to the patients. From this Oath, in 1847, the American Medical Association (AMA) developed a document, entitled the *Code of Medical Ethics* (Veatch, 1997). Over time, the *Code of Medical Ethics* was revised on multiple occasions to place a greater emphasis on the patients, which led to the establishment of the four pillars of medical ethics (Veatch, 1997). These four principles include: autonomy, beneficence, non-maleficence, and justice. Autonomy describes the right of the patient to be included in the decision making process (AlHasan, 2023). The principle of beneficence ensures that healthcare professionals act in the best interests of the patient, while the non-maleficence principle obligates healthcare

professionals to not harm the patient (AlHasan, 2023). Lastly, the principle of justice states that all patients should be given equitable access to healthcare resources (AlHasan, 2023).

The use of ML in diagnostic imaging processes raises many concerns regarding these four pillars. For instance, assume an algorithm was developed from a White male population and applied to diagnose a female population (AlHasan, 2023). The beneficence and nonmaleficence principles could be potentially violated as this algorithm can cause harm to the female population. Determining who should be responsible for this diagnostic error can be a challenging process. Some may argue that the programmers should be held accountable since they created a biased algorithm. Others may argue that the healthcare professionals should be held responsible as they are the ones who are employing the use of this technology. Furthermore, critics can argue that it should have been the physician's responsibility to learn the limitations of the algorithm. However, many of these algorithms are difficult to understand from a non-programmer perspective. A lack of understanding can often make it difficult for the physicians to explain to the patient how they came about making a certain diagnosis. This not only impacts patient-physician trust but may also violate the autonomy principle as patients may struggle to make informed decisions about their health (Farhud & Zokaei, 2021).

Research question and methods

This paper seeks to answer the following question: how do current attempts to integrate machine learning into patient diagnostic imaging processes reflect the four pillars of medical ethics? This research question is of paramount importance because it ensures that the integration of ML within imaging diagnostics upholds the current ethical framework in medicine. Additionally, this question guides the development of regulatory policies, which promote ethical

and responsible use of ML in medical diagnosis. To answer this question, I will conduct extensive literature review of academic publications that have been peer reviewed.

While performing literature review, I will analyze papers within academic journals such as the *Journal of Medical Artificial Intelligence* that highlight the applications and benefits associated with the implementation of ML into patient imaging diagnostic procedures. Additionally, I will use Trevor Pinch and Wiebe Bijker's theory, the Social Construction of Facts and Artefacts (SCOT), to identify the relevant social groups that are impacted by this technology. According to SCOT, these groups can include those who use the technology such as healthcare professionals and patients, the ones who develop the technology like the engineers, and those who enforce laws concerning the technology such as the regulatory bodies (Pinch & Bijker, 1984). I will then review publications written by the relevant social groups that address the impact of ML integration on the four pillars of medical ethics. Lastly, I will review academic papers within journals like the *Journal of Medical Ethics*, to identify cases where the four pillars of medical ethics were violated.

Conclusion

In my technical project, my team and I will develop and validate a deep learning neural network algorithm to accurately quantify the volume of thrombus burden that is still present within the patient. This algorithm enhances treatment for patients by offering important clinical indicators within PE, increases precision and efficiency, and reduces the diagnostic and surgical operating times. In my STS project, I will investigate how the integration of machine learning within patient diagnostic imaging procedures impacts the four pillars of medical ethics. This analysis can help guide the creation of regulatory policies that ensure the integration of ML within healthcare upholds the ethical framework developed by the medical community. Both my

technical and STS projects contribute to resolving the issue of diagnostic errors by creating a more accurate algorithm that abides by the ethical principles in medical practice.

References

AlHasan, A. (2023, February 8). Ethical Concerns Grow as AI Takes on Greater Decision-Making Role. *American College of Surgeons*. https://www.facs.org/for-medical-professionals/news-publications/news-and-articles/bulletin/2023/february-2023-volume-108-issue-2/ethical-concerns-grow-as-ai-takes-on-greater-decision-making-role/

Amisha, Malik, P., Pathania, M., & Rathaur, V. (2019). Overview of artificial intelligence in medicine. *Journal of Family Medicine and Primary Care*, *8*(7), 2328. https://doi.org/10.4103/jfmpc.jfmpc_440_19

Choy, G., Khalilzadeh, O., Michalski, M., Do, S., Samir, A. E., Pianykh, O. S., Geis, J. R., Pandharipande, P. V., Brink, J. A., & Dreyer, K. J. (2018). Current Applications and Future Impact of Machine Learning in Radiology. *Radiology*, *288*(2), 318–328. https://doi.org/10.1148/radiol.2018171820

Cuocolo, R., Cipullo, M. B., Stanzione, A., Romeo, V., Green, R., Cantoni, V., Ponsiglione, A., Ugga, L., & Imbriaco, M. (2020). Machine learning for the identification of clinically significant prostate cancer on MRI: A meta-analysis. *European Radiology*, *30*(12), 6877–6887. https://doi.org/10.1007/s00330-020-07027-w

Dilsizian, S. E., & Siegel, E. L. (2014). Artificial Intelligence in Medicine and Cardiac Imaging: Harnessing Big Data and Advanced Computing to Provide Personalized Medical Diagnosis and Treatment. *Current Cardiology Reports*, *16*(1), 441. https://doi.org/10.1007/s11886-013-0441-8

Farhud, D. D., & Zokaei, S. (2021). Ethical Issues of Artificial Intelligence in Medicine and Healthcare. *Iranian Journal of Public Health*. https://doi.org/10.18502/ijph.v50i11.7600

Li, W. T., Ma, J., Shende, N., Castaneda, G., Chakladar, J., Tsai, J. C., Apostol, L., Honda, C. O., Xu, J., Wong, L. M., Zhang, T., Lee, A., Gnanasekar, A., Honda, T. K., Kuo, S. Z., Yu, M. A., Chang, E. Y., Rajasekaran, M. " R., & Ongkeko, W. M. (2020). Using machine learning of clinical data to diagnose COVID-19: A systematic review and meta-analysis. *BMC Medical Informatics and Decision Making*, *20*(1), 247. https://doi.org/10.1186/s12911-020-01266-z

Liu, Z., Yuan, H., & Wang, H. (2022). CAM-Wnet: An effective solution for accurate pulmonary embolism segmentation. *Medical Physics*, *49*(8), 5294–5303. https://doi.org/10.1002/mp.15719

Pinch, T. J., & Bijker, W. E. (1984). The Social Construction of Facts and Artefacts: Or How the Sociology of Science and the Sociology of Technology might Benefit Each Other. *Social Studies of Science*, *14*(3), 399–441. https://doi.org/10.1177/030631284014003004

Ricotta, J. J., Pagan, J., Xenos, M., Alemu, Y., Einav, S., & Bluestein, D. (2008). Cardiovascular disease management: The need for better diagnostics. *Medical & Biological Engineering & Computing*, *46*(11), 1059–1068. https://doi.org/10.1007/s11517-008-0416-x

Topff, L., Ranschaert, E. R., Bartels-Rutten, A., Negoita, A., Menezes, R., Beets-Tan, R. G. H., & Visser, J. J. (2023). Artificial Intelligence Tool for Detection and Worklist Prioritization Reduces Time to Diagnosis of Incidental Pulmonary Embolism at CT. *Radiology: Cardiothoracic Imaging*, *5*(2), e220163. https://doi.org/10.1148/ryct.220163

Veatch, R. M. (1997). Medical Ethics: An Introduction. In J. Burns (Ed.), *Medical Ethics* (2nd ed., pp. 1- 27). Jones & Bartlett Learning

Wible, B. C., Buckley, J. R., Cho, K. H., Bunte, M. C., Saucier, N. A., & Borsa, J. J. (2019). Safety and Efficacy of Acute Pulmonary Embolism Treated via Large-Bore Aspiration

Mechanical Thrombectomy Using the Inari FlowTriever Device. *Journal of Vascular and Interventional Radiology*, *30*(9), 1370–1375. https://doi.org/10.1016/j.jvir.2019.05.024