THREE-DIMENSIONAL LUNG VOLUME MODELING FROM TWO-DIMENSIONAL IMAGING

FEAR OF GENETIC DISCRIMINATION

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
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November 2, 2020

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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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In 1990, the United States government created the Human Genome Project to form a dedicated body whose purpose was to map the entire human genome. DNA sequencing technology continued to improve and by 2000 nearly the entire human genome had been sequenced (Collins & McKusick, 2001, p. 540). As scientists discovered more about DNA, the ability for people to have their own DNA tested increased as well. Private companies began to provide options for people to obtain genetic testing information in the mid 2000s (Borry, Cornel, & Howard, 2012, p. 101). Genetic testing has the potential to improve the health and livelihoods of many. People could better modify risk factors according to genetic risk stratification, receive earlier care for diseases, or have "designer" drugs created specifically for them based on their genes (Collins & McKusick, 2001, p. 540). Although genetic testing provides great promise, public hesitation and fear regarding its consequences exist. Fear of genetic discrimination from health insurance companies is a common reason for people to not support genetic testing or to forego the option entirely (Allain, Friedman, & Senter, 2012, p. 640). Genetic testing offers potential life altering benefits but the presence of public fear could restrict the technology's capability. The STS research involved in this project will analyze the public's fear surrounding genetic testing and if methods exist to mitigate it.

The technical side of the project aims to create a better way for physicians to determine treatment plans for patients with early onset scoliosis (EOS), which in roughly two thirds of surgical cases is principally caused by genetics (Gao et al., 2014, p. 325). Additionally, Gao et al. (2014) aimed to find genetic mutations that lead to scoliosis and provided evidence that genetic mutations could be the cause of cases with no known epidemiology (p. 329). Early onset scoliosis patients that can be diagnosed due to their genetic data will be affected by the ways insurance companies will be allowed to use this information. Currently, there is not an exact

guideline for physicians on how to treat EOS (Cunin, 2015, p.S117). The technical will attempt to build an algorithm that will help physicians choose the optimal treatment plan for EOS patients by providing the patient's total lung capacity.

Both the technical and STS projects aim to provide better treatment to patients. Although the two sides are loosely coupled, research into the fear of genetic discrimination could provide benefits to the patients the technical project aims to help. The technical and STS portions will be conducted over the fall 2020 and spring 2021 semesters.

THREE DIMENSIONAL MODELING OF LUNGS FROM TWO DIMENSIONAL IMAGES

Early onset scoliosis (EOS) is a class of scoliosis, caused by a curve in the spine, that occurs before 8-10 years of age (Scoliosis Research Society, 2014). While the overall prevalence of EOS is unknown, scoliosis affects two to three percent of the US population. Although EOS is a rare condition, a treatment plan needs to be created for each patient. If left untreated, EOS commonly leads to death due to pulmonary complications (Scoliosis Research Society, 2014). Non-surgical options are initially recommended to treat EOS to slow the progression of the disease (Cunin, 2015, p. S117). However, the case may become severe and surgical intervention is necessary. Spinal fusion, which corrects the spinal deformity and curvature seen in scoliosis patients by placing two metal rods along the spine to force straightening, is the common surgical option. If performed too early, the patient can develop restrictive pulmonary disease (Karol, 2012, p. 1326). For this reason, spinal fusion is not a routine procedure at a young age. In order to proceed, it is crucial to determine the total lung capacity (TLC). TLC allows the physician to determine if the patient will have proper pulmonary function after spinal fusion surgery. Two common methods for measuring TLC are pulmonary function testing (PFT) and computed

tomography (CT) (Delgado & Bajaj, 2020). However, there are drawbacks to these methods. It is difficult for young children or those with disabilities to perform the PFT properly. CT, on the other hand, is relatively expensive, subjects patients to roughly ten times the amount of radiation of an X-ray, and children with disabilities may require a sedative to sit still for the duration of the scan (Kilbaugh, 2010, p. 5; Mettler, 2008, p. 254). The current options for determining TLC offer no clear set of rules or indications to perform surgery. Instead, the best option is to rely on the doctor's expertise and experience (Cunin, 2015, p. S117).

Supervised by Dr. Keith Bachmann, Orthopedic Surgeon at University of Virginia Health, Biomedical Engineers Will Farley, Sam Schach and I aim to develop an algorithm that will provide a three dimensional model of the lungs from two dimensional X-ray images. While X-rays may not be able to identify the lungs, they do display the rib cage. If the volume of the mediastinum, the central portion of the thoracic cavity that is not the lungs, is subtracted from the volume of the chest cavity, total lung capacity (TLC) will be calculated.

A convolutional neural network (CNN) will be used to determine the rib cage and mediastinum volumes. CNNs have been used in other medical fields to identify objects in various types of images (Anwar et al., 2018, p. 226). Specifically, our project will use a CNN used by a group of bioinformatics researchers to identify parts of the rib cage (Wessel & Heinrich, 2019). This study had some success but only used posterior X-ray images to identify the ribs, as seen in Figure 1, on page 4.

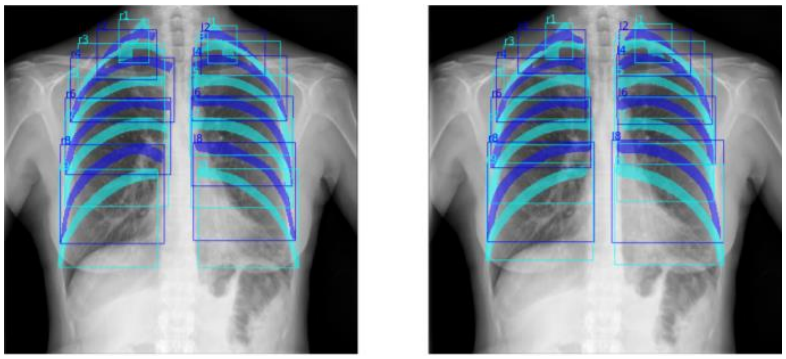

Figure 1: Automated rib identification: A convolutional neural network (CNN) was used to identify the rib cage from posterior X-ray images. On the left, the actual rib cage is shown and on the right, the predicted rib cage obtained from the CNN is shown (Wessel & Heinrich, 2019).

Through using both posterior and lateral X-ray images, we believe a three dimensional model of the rib cage can be created. The CNN will be trained on a collection of patient X-ray images Dr. Bachmann has given us. If the algorithm can give physicians an accurate TLC value, their ability to determine the best care for patients will be improved. The technical project will culminate in a scholarly article.

FEAR OF GENETIC DISCRIMINATION

If the technical project is successful, it will aid physicians in treating early onset scoliosis patients, which can often be attributed to genetics (Gao et al., 2014). Although genetic testing is currently only used for specific genes and rare conditions, the National Institutes of Health predicts it will reach a point where it will cost less than $1,000 to sequence the entire genome (National Institutes of Health, n.d.) As expenses decrease, the use of genetic testing will increase. Through genetic testing, people can identify diseases they have or are at more risk of developing. This information could lead to early treatment of diseases or allow people to make lifestyle decisions that could mitigate the problems associated with various diseases (Belisle-Pipon, Vayena, Green, & Cohen, 2019, p. 1198). Genetic testing also provides the possibility of unique and improved treatment for each patient (Nill, Laczniak, & Thistle, 2019, p. 105).

Although genetic testing provides great promise, people are hesitant to undergo testing due to fear of genetic discrimination. Specifically, people expect that if they get a genetic test their family and them will be forced to pay increased amounts for health insurance (Wauters & Van Hoyweghen, 2016, p. 279). This fear leads to some people foregoing genetic tests despite the potential benefits (Allain et al., 2012, p. 640). Even those who know they are predisposed to a certain condition may make the conscious choice to not get tested. In a specific case study on breast cancer, a group of women who had over 20% chance of developing breast cancer decided to not get tested specifically citing insurance genetic discrimination as the reason (Armstrong et al., 2003, p. 362). However, given these fears, Armstrong et al. (2003) found no evidence to show that insurance companies were using genetic information as a tool to change insurance premiums (p. 362). This raises the question why does the public fear genetic discrimination from insurance companies if there is a lack of evidence?

On the other side of this problem, insurance providers fear that without genetic testing they put themselves at financial risk (Nill et al., 2019, p. 114). Adverse selection is the instance where people who are at greater risk will continue to buy insurance while those at low risk are more likely to not get insured (Nill et al., 2019, 114). This creates financial risk for companies because, in an extreme case, they will only be providing insurance to those who will need to cash in on their plans to cover their medical expenses. In the above case concerning breast cancer, the women involved were likely to alter their insurance plans due to their genetic test results (Armstrong et al., 2003, p. 363). Therefore, insurance companies do have credible reasons to fear market failure.

If the current climate surrounding genetic testing continues to exist, the public risk losing the benefits genetic testing can provide. Another large barrier to the success of this technology is

the lack of understanding of genetic testing legislation. For instance, the United States government passed the Genetic Information Nondiscrimination Act (GINA) of 2008, which explicitly protects people from discrimination from health insurance companies. The act states that insurance companies can not use genetic testing information to deny coverage or make premium decisions (National Institutes of Health, 2020). Even after the enactment of this policy, people still chose to not get tested due to fear of discrimination (Allain et al., 2012, p. 640). Allain et al. (2012) stated that a lack of knowledge of the current legislature could be the reason for the continued presence of fear (p. 641). Additionally, misunderstanding exists among the government officials whose job is to enforce insurance legislation (Golinghorst & Prince, 2019, p. 3). Different states have different laws on how genetic information can be handled by health insurance companies. Golinghorst and Prince (2019) suggested this complicated legislative reality has led to their misunderstanding (p. 5). There is also little evidence of communication between the public and the policy enforcers. The fear exists, but state insurance commissioners do not hear of it directly from their constituents. A line of communication is needed between the state commissioners and the public. Additionally, it is imperative that both the public and policy enforcers obtain a better understanding of the genetic testing legislature for the promises of genetic testing to substantialize.

ENGINEER: ENFORCE COMMUNICATION

For genetic testing to be used to its fullest capabilities, a closer look at how society interacts with this technology is necessary. The engineers who are developing genetic testing technology will need to ensure its success. The success of genetic testing relies on the creation of a Social Construction of Technology (SCOT) model (Pinch & Bijker, 1987), as shown in Figure 2 on page 7.

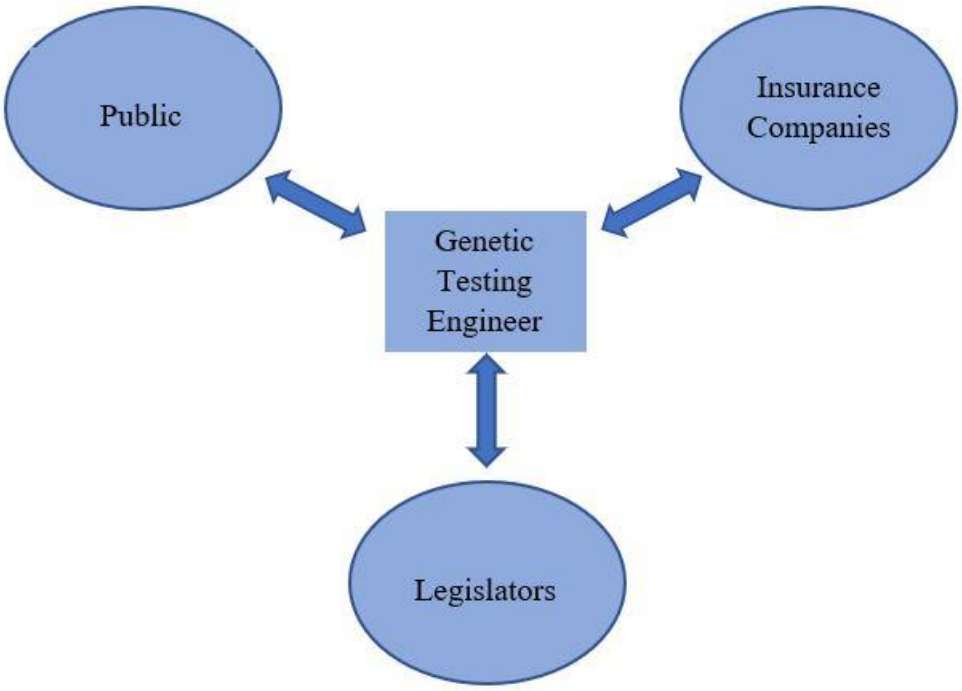

Figure 2: Genetic testing SCOT model: The engineer at the center is expected to take each actor's interests into account to produce a successful genetic testing product (Adapted by Anthony Albini (2020) from W. B. Carlson, 2007).

This Social Construction of Technology (SCOT) model emphasizes how not only the engineer will shape genetic testing technology but also the social groups involved. The public or policyholders, insurance companies, and legislators will affect how engineers will develop genetic testing technology. As mentioned previously, these social groups have already altered the technology. Genetic testing is at a point where society may lose its potential because of the actions of the social groups identified. Engineers will need to keep in mind the values of each of the groups in this model to allow genetic testing to succeed. As engineers continue to develop genetic testing to the point it becomes cost effective for widespread usage, they will need to effectively communicate with each group. The policyholder's suspicion of suffering from genetic discrimination, the health insurance industry's fear of market failure, and the legislative wish to protect its constituents need to all be considered.

Rogers et al. (1996) outlines a study of the STOP AIDS campaign where the creation of focus groups allowed information to spread through targeted communities (p. 10-11). A system that the engineer should try to obtain through creating focus groups in which the three groups can communicate their concerns and values is shown in Figure 3.

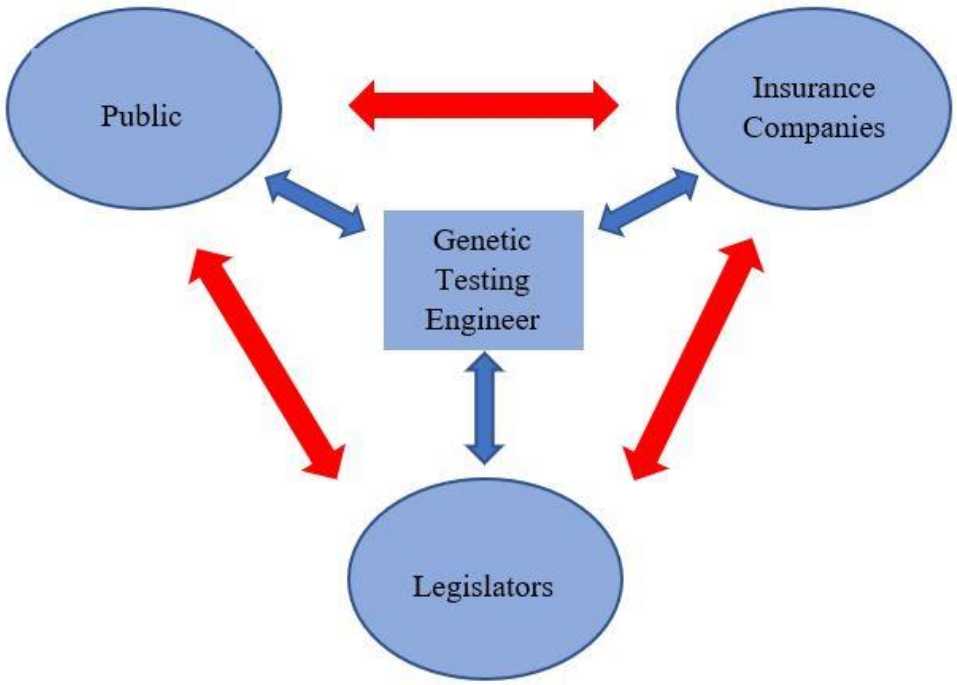

Figure 3: Genetic testing SCOT model with improved communication: Similar to the previous SCOT figure except the red arrows signify the engineer focusing on improving communication between the actors (Albini, 2020).

The focus of the engineer should be to consider each groups values but also creating communication networks between the groups. As Golinghorst and Prince (2019) stated, if communication between the state commissioners of insurance and the public increases, the benefits of genetic testing can be allowed to occur (p. 6). Increase of feedback should not end here, legislators should also consider the values of the insurance industry. Additionally, insurance companies will need to consider the values of their policyholders and vice versa. With respect to the AIDS pandemic, once relevant social groups communicated, the overall public health improved (Rogers et al., 1996, 10-11). If genetic testing engineers focus on building

communication networks between the social groups hopefully similar public health benefits can be achieved. The STS research project will culminate in a scholarly article examining the public's suspicion of genetic testing and how improved systems of communication could potentially change the current situation.

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