**Prospectus**

**Three-Dimensional Modeling of Lung Volumes in Scoliosis**
(Technical Topic)

**Actor Network Theory and the Failure of the Exubera Insulin Inhaler**
(STS Topic)


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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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## Sociotechnical Problem

Adolescent idiopathic scoliosis (AIS) accounts for 85% of the general population scoliosis cases worldwide (Tsiligiannis & Grivas, 2012). Due to the deformity of the spine and rib cage in AIS, impaired lung function is a common complication (Fujita et al., 2019). Patients diagnosed with AIS require a spinal fusion (SF) surgery to correct for spinal curvature. In remedying the spine, SF surgery also prevents further deterioration of lung function by restricting chest space for lung growth (Kumano & Tsuyama, 1982). However, limiting lung growth also limits the maximal air intake by the lungs; as a result, healthcare providers face the dilemma of balancing lung growth for optimal lung intake air capacity and the urgency of spinal fusion surgery. Thus, physicians require a method to measure total lung volume in order to determine when to perform SF surgery on patients. Currently, clinicians use pulmonary function testing (PFT) and computed tomography (CT) to calculate lung volume. Although these techniques are functional, many AIS patients are too young to comply to PFT protocol and exposure of large-dose radiation from CT scans are dangerous (Enright et al., 2000; Fujita et al., 2019; Seoud, Cheriet, Labelle, & Dansereau, 2011). Therefore, medical providers require a safer and equally accurate method to determine total lung volume. The technical solution to this problem is to develop a 3-dimensional (3D) computational model of the lungs that calculates total lung volume from simple X-rays of AIS patients.

However, a technical solution alone is insufficient in resolving the full spectrum of the issue. In order for the technical project to succeed, we also need to address the social, economic, and political factors that influence the fate of the 3D lung model. Specifically, we need a better understanding about how technologies function within larger networks comprised of various kinds of actors, each of which contributes to the project's prosperity (Callon, 1987). At the same time, these networks may also be instrumental in the failure of technologies, such as in the case of the Exubera insulin inhaler. Exubera, created by a pharmaceutical company called Pfizer, was the first inhaled insulin product sold on the market but was pulled from the shelves after only a year in retail (Mack, 2007). While poor economic planning and long-term health effects played a role in Exubera's failure, other factors such as the unstable networks formed by Pfizer and rogue actors within the network played critical roles in the product's demise. By considering the impact of different actors in the network, we gain insight into how human and nonhuman factors destabilized the network, leading to the failure of Exubera.

To effectively redesign a safer method for determining lung volume, both the technical and social aspects are crucial in addressing the limitations of current medical treatments for AIS patients. Below, I outline a technical process for innovating a computational method to measure total lung volume in patients. I also use actor-network theory and Callon's concept of translation to analyze how human and nonhuman actors contributed to the destabilization of the Exubera network, ultimately gaining insight on the importance of actor networks for the success of technical solutions.

## Technical Problem

Adolescent idiopathic scoliosis (AIS) is the most common 3D deformity of the spine and rib cage in children (Grenier, Parent, & Cheriet, 2013; Tsiligiannis & Grivas, 2012). Among the adolescent population, the curving of the spine not only leads to postural problems during growth, but also to lung complications (Seoud et al., 2011). Studies show that the rib cage in AIS patients is narrower than in normal counterparts. Consequently, the impairment of normal chest development leads to insufficient space available for lung growth and results in restrictive lung diseases (Tsiligiannis & Grivas, 2012). In order to prevent deterioration of lung function in AIS patients, healthcare providers perform spinal fusion (SF) surgery as a corrective measure for spinal deformation (Fujita et al., 2019; Kumano & Tsuyama, 1982). However, despite studies finding improvement in lung function post SF operation, the maximum amount of air intake needed to support the patient's body shows no significant improvements (Fu et al., 2015; Kumano & Tsuyama, 1982). As a result, medical providers face the challenge of balancing achievement of maximal lung volume in AIS patients for best quality of life and the urgency for SF surgery to correct for detrimental consequences. Therefore, physicians require a clinical technique that assesses patient total lung volumes to aid in determining the ideal timeline for SF surgery action (Grenier et al., 2013).

Currently, there are two methods to determine total lung capacity in AIS patients: pulmonary function testing (PFT) and computed tomography (CT). Pulmonary function testing is used to evaluate the effect of lung diseases on respiratory function (Fujita et al., 2019). However, identification of AIS and lung function occurs early in adolescence when patients are too young to cooperate with components of the PFT protocol such as expiring into the device (Enright et al., 2000; Fujita et al., 2019). Computed tomography accurately measures total lung volume by producing cross sectional images of the body, but its high dosage exposure of radiation is unsuitable and dangerous for children (Fujita et al., 2019; Seoud et al., 2011). Thus, medical providers are in need of a novel method to safely estimate lung volumes of AIS patients. Development of a computational lung model could provide a safer, equivalently accurate way to measure total lung capacity, as well as improve the quality and accessibility of care for pediatric patients. For healthcare providers, it could warrant the uncertainties of SF surgical timing and allow them to provide better healthcare.

The goal of this technical project is to develop a 3D computational lung model that can determine total lung volume from X-rays of AIS patients. There are many milestones required to reach the objective. First, a constant will be determined by analysis of patient CT scans to account for chest volume that is not part of the lungs. Additionally, constants will be constructed for a wide patient demographic based on age, height, sex, and weight. Next, a 3D model of the rib cage paired with artificial intelligence will be morphed to match patient X-rays. From this model, the patient's full chest volume will be calculated. Finally, the constant will be subtracted from the chest volume to produce the total lung volume, ultimately creating a safer and standardized way to track lung progression of AIS patients.

## STS Problem

Diabetes affects approximately 30.3 million Americans and is a disease where the body does not produce enough insulin resulting in high blood glucose levels (Diabetes Research Institute, n.d.). In order to treat diabetes, patients undergo insulin therapy. One popular method of insulin delivery is with a needle and syringe (Smith-Marsh, 2019). Unfortunately, insulin effectiveness and patient compliance via syringe delivery is low due to improper injection technique as well as psychological barriers such as needle phobia and being misrepresented as a drug addict (Heinemann, 2008; Oleck, Kassam, & Goldman, 2016). Consequently, a pharmaceutical company called Pfizer developed an alternative insulin delivery method: inhaled powder insulin branded Exubera (Borja, Daniel, & Tourtelot, 2007). Exubera was the first inhaled insulin to be approved by the U.S. Food and Drug Administration in 2006. Functionally, it was noninferior to subcutaneous syringe injections in decreasing blood sugar levels of diabetic patients (Oleck et al., 2016).

Unfortunately, after less than a year in retail, Exubera was pulled from the market due to poor sales. Pfizer estimated selling $1 to $4 billion worth of its product but only vended off $12 million worth, costing the company $2.8 billion dollars (Mack, 2007). Many scholars study the failure of Exubera and pinpoint its demise on Pfizer's poor planning in two main areas: economic cost efficiency and safety concerns. Despite equivalent effectiveness, Exubera was not cost-effective as replacement insulin blisters for Exubera costed more than a vial of liquid insulin (Borja et al., 2007). Furthermore, adverse side effects such as hypoglycemia, respiratory infections, and lung cancer appeared in long term patients on Exubera. Many scientists believed that the size and quality of the insulin powder particles caused these respiratory consequences and its inevitable downfall (Oleck et al., 2016). While scholars recognize the importance of Pfizer's responsibility for the medical device disaster, they do not give enough attention to the other actors who played critical roles in the failure of Exubera. Other actors of the network such as physicians and nurses, insurance companies, manufactures, patients, politicians, and even the device itself were also crucial in marketing Exubera. If we continue to think that only Pfizer was responsible for the project's failure, we lose insight into how other actors influenced the fate of Exubera. Considering human and nonhuman factors such as education, corporate profit, political agendas, and aesthetics highlight the importance of both quantitative and qualitative research in innovating successful medical devices.

To examine the influence of various actors in the failure of Exubera, I will use the science, technology, and society (STS) concept of actor-network theory (ANT), which analyzes the connection of power dynamics between human and nonhuman actors associated in a heterogenous network aimed at accomplishing a goal (Cressman, 2009). Specifically, I will use Michel Callon's concept of translation, which describes the process of forming and maintain an actor network undertaken by a network builder (Callon, 1987). Drawing on ANT and the concept of translation, I argue that it was Pfizer in conjunction with other human and nonhuman actors that played key roles in the failure of Exubera to form a successful network.

## Conclusion

In this paper, the technical report will deliver a novel solution using a 3D computational model of the lungs to calculate total lung capacity in adolescent idiopathic scoliosis patients. This method will accurately and safely aid healthcare providers in determining the best time for patients to undergo spinal fusion surgery to correct for spinal curvature. Additionally, the STS research paper will use actor-network theory and Callon's concept of translation to examine how various human and nonhuman actors influence the stability of a technological network. Specifically, these concepts will be applied to analyze the roles of actors in destabilizing the Exubera network, which led to the demise of the inhaled insulin product.

Ultimately, the results of the technical and STS project will help to better understand the broader sociotechnical issue of how technologies function within larger networks composed of numerous actors, each of which contributes to the project's success or, in certain cases, failure. This insight could help pioneer a comprehensive understanding of how human and nonhuman factors affect the accessibility of healthcare systems through the formation and stabilization of technological networks.

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