

Quantifying Myocyte Infiltration of an Electro Spun P4HB Mesh

The Role of Physician Education and Incentives in Physician Decision Making

A Thesis Prospectus

In STS 4500

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Bachelor of Science in Biomedical Engineering

By

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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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Introduction:

The healthcare system is multi-faceted and complex. It not only includes patients and healthcare workers, but is intertwined with medical devices, drugs, hospital systems, and the bureaucracy of medicine. My technical research project focuses on the research and development of medical devices – specifically surgical mesh for hernia repair. The current repair options leave patients with weak abdominal muscles, unable to do significant physical activity. My technical team is looking into an electro spun version of a current bioresorbable material used in hernia repair. This material is called poly-4-hydroxybutyrate (P4HB) which degrades to 4HB, a normal and biocompatible compound found naturally occurring in the body (Utsunomia et al., 2020). We are looking at the alignment of electro spun fibers as a determining factor for myocyte (muscle cell) integration. This research may serve as an early indication that hernia recovery can be improved for millions of people around the world.

The focus of my STS research paper, physician education, is related to my technical project in that it involves the adoption of new medical devices and treatments by surgeons. Physician education is a vital part of the healthcare system; it involves pharma and medical device companies sending out representatives to educate physicians on new drugs or medical devices. This education can involve a paid dinner to catch the full attention of private practice physicians who are busy seeing patients all day, but has been stretched to include paying for physicians' trips to conferences and paid vacations in order to encourage the writing of more prescriptions.

Drawing the line between what has gone too far in the name of physician education to help patients is a complicated task, as there are many pieces at play in this network. I will be utilizing actor-network theory to analyze how education and incentives, pharmacists, physicians, and legislation form an interconnected network.

Technical Report:

My technical project is looking at poly-4-hydroxybutyrate (P4HB) electro spun mesh for hernia repair. A hernia is a common medical complication mostly in the elderly, affecting around one million people per year. A hernia occurs when an organ or tissue pushes through an opening in muscle tissue, and can be often be seen visually protruding outside of the body. Hernias almost always require surgery for repair(Millikan, 2003). The most common repair process is the use of hernia mesh, brand name Phasix, composed of P4HB. P4HB is a bioresorbable material that is broken down into a naturally occurring metabolite in the body, 4HB. Unfortunately, the implementation of the mesh does not provide a full recovery for many patients. Surgical hernia repairs often result in the loss of mobility and weakness, hindering patients from returning to their full physical activities(*Characterization of Poly-4-Hydroxybutyrate Mesh for Hernia Repair Applications - ScienceDirect*, n.d.).

We believe that electrospinning hernia mesh will provide a tunability of fiber alignment and pore size that may promote a more complete muscle recovery.

The goal of this work is to investigate the interaction between electro spun poly-4-hydroxybutyrate (P4HB) mesh and myocytes and/or neural progenitor cells.

Aim 1: Fully understand the limitations and implications of current hernia repair methods

- Conduct a literature review of the current biomaterials used in hernia repair
- Determine which properties of biomaterials are necessary for muscle repair: pore size, fiber thickness, scaffold design
- Synthesize findings, determine what has been done previously, both successful and unsuccessful. Identify approaches and strategies for hernia repair biomaterials that have not been explored yet

Aim 2: Examine how the myocytes interact with the P4HB mesh

- Develop good cell culture practice (GCCP) for seeding myocytes to ensure reliable and reproducible results
- Establish criteria for what constitutes a successful interaction between the myocytes and P4HB mesh. Determine how muscle regeneration will be quantified
- Characterize how scaffold design affects viability, morphology, migration, proliferation, and functional marker expression

Aim 3: Compare P4HB findings with other hernia repair meshes on the market

- Drawing on research from Aim 1, analyze how P4HB compares to other available hernia repair meshes at a similar stage in their development
- What are the advantages of P4HB, how will these findings drive hernia repair mesh research forward?
- Identify areas where the P4HB mesh could be improved, where did it underperform

Our team has completed a literature search of the current hernia repair methods and why they are failing. Additionally, we are currently writing a protocol to be used in our experiment for myocyte quantification and qualification.

A successful project will yield: the establishment of quantifiable metrics of a positive interaction between P4HB and myocytes, determination of if electro spun P4HB met these criteria and has promise as a scaffold for muscle regeneration, and the identification of optimal initial design specifications of a hernia mesh. We believe the outcome of this project will eventually be able to help millions of hernia patients worldwide recover more fully with increased muscle mobility following surgery.

STS Prospectus

Since the beginnings of the modern practice of medicine, there has been a business associated with medicine. With the growth of medical drug and device companies within the last one hundred years, it is common practice for representatives of these companies to meet with physicians to educate them on the company's products. The main goal of this exchange is to educate physicians with an added benefit of the physicians being more likely to prescribe their product as a result of the education.

The issue with this education is that it historically entails paying for outings (meals, golf, etc.) with physicians to get an uninterrupted hour. The notion of physician education is a highly contentious one, as it becomes difficult to draw the line between what is simply education versus what is over-compensation. While direct monetary payment for the purpose of convincing physicians to prescribe is relatively rare and agreed upon to be unethical, it is harder to make the distinction for meetings of smaller monetary cost.

The Affordable Care Act of 2010 attempted to mitigate inappropriate payment that directly influences prescribing. Centers for Medicare and Medicaid (CMS) payments, an official website of the United States Government, was set up as part of the 2010 Affordable Care Act. It is a public database that houses records of payments that drug and medical device companies make to physicians to promote a more transparent and accessible healthcare system.

Physician education, whether a transfer of money is associated or not, *will* impact a physician's decision making. I will be investigating the roles among CMS Payments and 2010 Affordable Care Act, physicians, pharmacists, and pharma and medical device companies in physician education and medical decisions. Similar to Angèle Bilodeau's piece in Health Promotion International, I will be utilizing Actor Network Theory to examine how these players are interconnected. Bilodeau focuses on the effectiveness of public health interventions (Bilodeau & Potvin, 2018). Similarly, I will be looking at the effect of the public health intervention of legislation concerning the Affordable Care Act of 2010 on the network. At

the paper's end, the reader should have a strong understanding of the interconnectedness of physician education and the influence that pharma and medical device companies can have.

Education and Incentives from Pharma and Medical Device Companies

Education and incentives are an important actor in this network; they are the push for physicians to prescribe one drug or device over another. These incentives can be disguised under the notion of physician education. Most of the time, education is just that -- education. Sometimes, though, it has been stretched to catered dinners, trips to conferences, golf outings, and even paid vacations for physicians and their families.

Although it is not common, there have been multiple instances of a clear undue pharma influence in inappropriate prescribing. One such instance is Avenir Pharmaceuticals targeting the elderly at long term care (LTC) facilities, knowing that their drug Nuedexta was not appropriate of the needs of all of the patients. It was reported in 2019 that one physician, a paid speaker for Nuedexta, had entire units of patients on the drug in the LTC where he worked (*Pharmaceutical Company Targeting Elderly Victims Admits to Paying Kickbacks, Resolves Related False Claims Act Violations*, 2019). It's important to highlight instances such as this one to emphasize that though they are rare, these payoffs do occur – and they have direct consequences on patients.

Pharmacists

Pharmacists are a key player and have an outside perspective; they are not a party that typically receives money or incentives for writing more prescriptions of a certain drug, though clinical pharmacists interact with physicians consistently.

I interviewed David Pass, PharmD, regarding his views on physician education and how it's evolved over the past 30 years. David graduated the Philadelphia College of Pharmacy in 1993, obtaining his undergraduate and Doctor of Pharmacy degree. Dr. Pass worked in marketing for multiple big pharma companies as well as a clinical pharmacist on the weekends. David's role was in marketing, but he was aware of the education that took place between the company and physicians.

He states that the notion of taking physicians out to dinner was never a form of payment; physicians in private practice have very little free time during the day, so taking them out to dinner is a way to have their full attention for an hour to educate them. (*Interview with Dr. David Pass PharmD, 6 October 2021, personal communication, n.d.*)¹.

For a more robust understanding of pharmacists' views on physician education, I interviewed Michael Pass, a retired Pharmacist and Business owner in Sarasota, Florida. Mr. Pass practiced pharmacy for 55 years at his small business, Family Pharmacy, before retiring in the early 2000s. Mr. Pass' view on physician payment is a unique perspective because he occasionally took physicians out to dinner. This was viewed as common practice at the time, and was very much legal. Reiterating what David Pass stated, Michael Pass wanted an uninterrupted moment with physicians to educate them on the compounded products he made. The benefit of this dedicated time is that the physicians were more likely to suggest Family Pharmacy to their patients to get specific products he compounded (*Interview with Dr. Michael Pass PharmD, personal communication, October 6, 2021*)¹.

Private Practice Physicians

Physicians in private practice are the main players in this network. They are affected and influenced by all of the other players: the education and incentives, pharmacists, the Sunshine Act of the 2010 Affordable Care Act, and the CMS transparency requirement. Physicians in private practice are the

most relevant and specific type of physicians to look at, as they are not subject to strict hospital requirements concerning physician education.

I interviewed retired physician Dr. Eddie Papish for his take on physician education and incentives. Dr. Papish practiced medicine for over 50 years in a private practice setting, and then moved to clinical teaching for 10 years. Eddie was aware of other physicians receiving more expensive gifts, but said that a dinner or conference was the extent of any education he received, and was never in the form of direct monetary payment (*Interview with Dr. Edward H Papish DO, 6 October 2021.*, personal communication, n.d.)¹.

CMS Payments and The Affordable Care Act of 2010

The Affordable Care act of 2010 added an act specifically pointed at drug and medical device companies giving money or gifts to physicians (*The Physician Payments Sunshine Act / Health Affairs*, n.d.). The act, named the Physician Payments Sunshine Act (PPSA), requires medical product manufactures to disclose to the Centers for Medicare and Medicaid services (CMS) any financial compensations made to physicians or teaching hospitals. Additionally, it requires certain manufacturers and groups purchasing organizations (GPOs) to disclose any physician ownership or investment interests held in those companies.

The result of the Sunshine Act was the rollout of the CMS payments system. CMS is an online website dedicated to providing transparency with physician payoffs. Manufacturers of drugs, medical devices, biologics, and medical supplies and group purchasing organizations (GPOs) are responsible for reporting their physician payments into the system – a publicly available database (*Open Payments Data - CMS*, n.d.).

Despite the main sentiment of transparency, there are multiple loopholes in the CMS reporting system. One main loophole concerns catering large meals, where buffets can be reported differently than

individual paid meals for physicians. A second loophole is with “indirect” payments to physicians who serve as faculty for “certified” and “accredited” continuing medical education (CME) programs. It allows for money, as long as it is not directly given to the speaker/faculty member, to be unreported in the CMS system. These funds of unknown amounts can quickly add up to hundreds, thousands, even millions of dollars(Lichter, 2015). The figure below details the interconnected nature of the players in this network(left), and which relationships were affected by the Affordable Care Act of 2010(right).

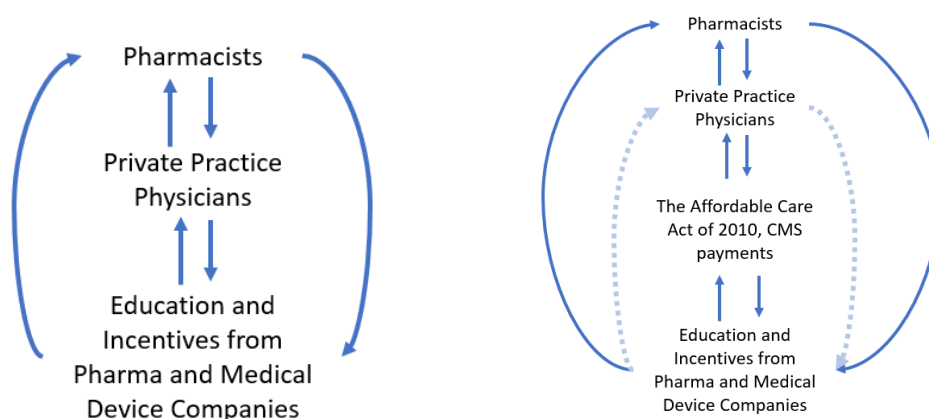


Figure 1: The Interconnected Network of Players Affected by the Affordable Care Act of 2010

Conclusion

Physician incentives have the power to corrupt a physician’s sound judgement, but Michael Pass put it best when he stated “There are good and bad people in every profession”. This sentiment holds true, as the majority of physicians agree to be educated by drug and medical device companies but do not let the money, dinners, or gifts make the prescribing decisions for them. The interconnected network of physicians in private practice, pharmacists, and education and incentives was altered by the passing of the Affordable Care Act of 2010; it stopped *some* unethical physician incentives by pharma and med device companies. This act requiring transparency of payments to physicians is a partial step in the right

direction; there is still work to be done to curb unjust incentives and payments for physicians affecting their clear decision making of thoughtful, fact-based care for patients.

Next Steps

In order to more fully understand this network of actors, I will continue to explore the role of patients, specifically how they are connected to physicians and CMS payments. This relationship between patients and physicians is vital to understand as it relates to care giving, diagnostics, and prescriptions. Additionally, I will qualify and quantify how patients have changed their private practice physician preferences based on the implementation of CMS payments.

Completion of both the technical Capstone project and the STS research project will occur by May 2022.

A combined timetable of work for the Capstone project and the STS Research paper is detailed below:

<i>Date</i>	<i>Capstone Item Completed</i>	<i>STS Item Accomplished</i>
November 2021	Continue literature search of current repair methods and their consequences Complete good cell culture training	Submit Prospectus to STS Professor and Capstone Advisor Receive Prospectus Sign-off from STS Professor and Capstone Advisor
December 2021	Receive testing material from Becton Dickinson Create a protocol for testing materials, design specs	Submit post prospectus evaluation
January 2022	Begin experimenting with mesh – quantifying myocyte infiltration	
February 2022	Continue mesh experiments and begin to compile data	Complete draft of Research Paper
March 2022	Finish compiling data Start to formulate conclusions about myocyte infiltration and alignment of fibers	
April 2022	Complete statistical analysis of	Submit Thesis Portfolio (end of April)

	Draft technical report, including conclusions on myocyte infiltration and alignment of fibers.	
May 2022	Submit technical report to Becton Dickinson and the University of Virginia	

Footnotes

1. The author has a personal relationship with the interviewees.

References

- Bilodeau, A., & Potvin, L. (2018). Unpacking complexity in public health interventions with the Actor–Network Theory. *Health Promotion International*, 33(1), 173–181.
<https://doi.org/10.1093/heapro/daw062>
- Characterization of poly-4-hydroxybutyrate mesh for hernia repair applications—ScienceDirect*. (n.d.). Retrieved October 14, 2021, from
https://www.sciencedirect.com/science/article/pii/S0022480413002382?casa_token=uU-eo1cDXS4AAAAA:uenjcO7I41LbVdBmPmadnLnsRO04pHvop4PgIjALDutYPdBEqOhRyVXPc4MX7iYPmf50uC8
- Interview with Dr. David Pass PharmD, 6 October 2021*. (n.d.). [Personal communication].
- Interview with Dr. Edward H Papish DO, 6 October 2021*. (n.d.). [Personal communication].
- Interview with Dr. Michael Pass PharmD*. (2021, October 6). [Personal communication].
- Lichter, P. R. (2015). Implications of the Sunshine Act—Revelations, Loopholes, and Impact. *Ophthalmology*, 122(4), 653–655. <https://doi.org/10.1016/j.ophtha.2014.12.029>
- Millikan, K. W. (2003). Incisional hernia repair. *Surgical Clinics*, 83(5), 1223–1234.
[https://doi.org/10.1016/S0039-6109\(03\)00129-4](https://doi.org/10.1016/S0039-6109(03)00129-4)
- Open Payments Data—CMS*. (n.d.). Retrieved October 4, 2021, from <https://openpaymentsdata.cms.gov/>
- Pharmaceutical Company Targeting Elderly Victims Admits to Paying Kickbacks, Resolves Related False Claims Act Violations*. (2019, September 26). <https://www.justice.gov/opa/pr/pharmaceutical-company-targeting-elderly-victims-admits-paying-kickbacks-resolves-related>
- The Physician Payments Sunshine Act | Health Affairs*. (n.d.). Retrieved October 6, 2021, from
<https://www.healthaffairs.org/doi/10.1377/hpb20141002.272302/full/>
- Utsunomia, C., Ren, Q., & Zinn, M. (2020). Poly(4-Hydroxybutyrate): Current State and Perspectives. *Frontiers in Bioengineering and Biotechnology*, 8, 257. <https://doi.org/10.3389/fbioe.2020.00257>