DEVELOPMENT OF A NOVEL FETAL HEART RATE MONITOR FOR MULTIPLE GESTATION PREGNANCIES

AN ANALYSIS OF THE THERANOS BLOOD ANALYZER VIA THE SOCIAL CONSTRUCTION OF TECHNOLOGY

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
Roman Ramirez

October 27, 2022

Technical Team Members:
Andrew Thede and Roman Ramirez

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

Rider Foley, Department of Engineering and Society

Dr. Kristen Naegle, Biomedical Engineering

Dr. Natasha Sheybani, Biomedical Engineering

Introduction

Dr. Naegle, a biomedical engineering professor at the University of Virginia and pregnant with twins, seeks a routine pregnancy checkup to gain information about their overall health. While nurses found the fetal heart rate (fHR) of one easy to monitor, they found the other was obstructed by the signal of the first fetus. Now a mother to two healthy twins, Dr. Naegle seeks to find a biomedical solution to the shortcomings of fHR monitors. This problem serves as the foundation and motivation for my capstone group to improve the clinical standard of fHR monitoring for multiple gestations or fetuses.

The current standard for external fHR monitors utilizes Doppler ultrasound (US), a sound-based technique to measure the distances of artifacts through a medium through specular reflection (Routh, 1996). However, the current standard of US fHRs lacks the ability to both identify and locate heart rates (HRs) of pregnancies of multiple gestations, or those carrying twins and higher (Giles, 1998). If such obstruction could be algorithmically reversed, healthcare would have an accessible, non-invasive, safe, gestation-independent method for measuring fetal heart rates. In addition, most fHR monitors secured around the waist also obstruct the lower back, which is the site where an epidural, a procedure to provide pain relief for labor and childbirth ("Epidural," 2021), is administered. This design choice presents a difficult situation for women, who would have to choose between an epidural and fHR monitoring. Although some may argue that women could choose an alternative monitoring method alongside an epidural, an improvement to the ultrasound-based method would provide greater healthcare access as an accessible and non-invasive method of fHR monitoring.

For these reasons, our capstone aim is to provide a method for monitoring fHRs of multiple gestations that provides access to the lower back. This technology will offer a safer,

more accessible–and ideally just as accurate–option compared to internal fHR monitoring. I will work with capstone partner Andrew Thede, and biomedical engineering advisors Dr. Naegle and Dr. Sheybani to design this device's components and components necessary for testing and verification. With accessibility in mind, my capstone team and I will determine an ideal transducer positioning and create an apparatus that holds this array, with human safety and the cost of materials in mind. Our work aims to produce a technology that is affordable, safe, accessible, and usable regardless of the number of fetuses in the womb, ultimately advancing the current field of multiple-gestation fetal heart rate monitoring.

The Multiple Gestation Fetal Heart Rate Monitor

Multiple gestation births account for around 3% to 4.5% of all births, which are often lighter in birth weight and smaller for their gestational age in comparison to singleton births (Kalikkot Thekkeveedu, Dankhara, Desai, Klar, & Patel, 2021). In addition, the mortality rate in black twin infants was double that of white twin infants in the United States (Waller, Ross, Hoskins, & Daling, 1993). People in urban communities have more access to care when compared to rural areas (Adams et al., 2022), and a disparity exists in the prenatal detection of congenital heart disease between urban and rural groups (Hill, Block, Tanem, & Frommelt, 2015). With these apparent health disparities in pregnancies, such healthcare gaps must be reduced by advancing technology that improves multiple gestation infant outcomes.

Doppler ultrasound (US) is the *de facto* standard technology for fHR monitoring in pregnant women (Hamelmann et al., 2020). Noninvasive fetal ECGs, such as US, provide just as accurate and safer results compared to invasive internal fetal monitoring, such as an intrauterine pressure catheter and fetal scalp electrode (Euliano et al., 2017). Although US fHR monitoring is

variable in design across various clinical models, most US fHR monitoring systems can be summarized in four parts (see Figure 1): the US transducer, Doppler signal processing, fHR extraction, and the display and presentation (Hamelmann et al., 2020).

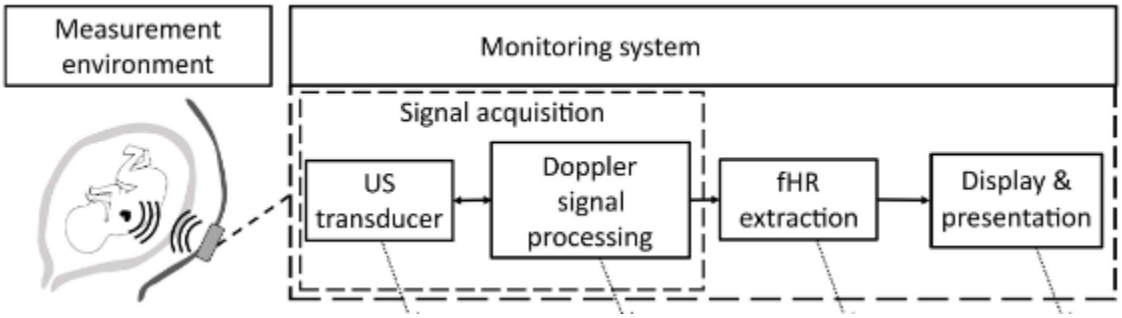

Figure 1. The overall summary of the clinical standard ultrasound fetal heart rate monitoring. (Hamelmann et al., 2020)

In the clinical standard, the problems this technology presents are two-fold; signal acquisition is clinically approved to acquire only a single fHR, and device adhesion to the mother is such that the lower back is obstructed. Portable monitoring systems focus only on a single heart; the presence of a second fHR would confound the signal of the first (Ayres-de-Campos, Stones, Theron, & the FIGO Safe Motherhood and Newborn Health Commitee, 2019). In addition, while some clinical monitors are handheld, those that are fastened to the mother provide a more accurate reading but render the lower back obstructed by its fastening device. Although signal accuracy is vital for the less accurate US method, blocking by this fastening device would interfere with an epidural. For these reasons, we aim to design a phantom gel–an acoustic replica–to mimic the womb environment, use this phantom gel to design an array of US

transducers to receive data, and develop an algorithm to filter, analyze, and identify simultaneous fHRs.

With these three deliverables, our method would be able to improve HR differentiation and eliminate obstruction problems of current clinical monitors. With a transducer array, an algorithm can approximate the location of the signal based on fHR signal distance and intensity (Hamelmann et al., 2016). Our array would be safe, producing a maximum intensity of 94 mW/cm^2, a safety threshold specified by FDA guidelines (Kollmann et al., 2013). Our work will make US fHR monitoring more accessible by designing the fastener for all body types and by preventing the obstruction of the lower back, will be cheaper and safer compared to internal fHR monitoring, and will advance the current clinical standard of US fHR monitoring by allowing multiple heart rates to be simultaneously monitored.

Some may argue that US signals are weaker than invasive methods and are even weaker in high-BMI individuals, which could promote a BMI-based disparity (Euliano et al., 2017). However, US–a noninvasive method–is a safer alternative, and we aim to design an fHR monitor with such biomedical disparities in mind.

Through the development of such a proposed technology, our capstone group seeks to understand its social construction of technology through the socio-technological relationships of another biomedical device: the Theranos blood analyzer.

The Social Construction of the Theranos Blood Analyzer

While my technical project aims to develop a novel fetal heart rate monitor for multiple gestation pregnancies, I seek to analyze the influence of various social groups on the TBA through Bijker's framework SCOT and how such socio-technological relationships could

improve in the development of future volumetric absorptive microsampling (VAM) devices. Under SCOT, a theory proposed by Bijker and supported by social constructivists, it is argued that the Theranos blood analyzer did not *influence* but rather was *influenced* by key social groups, both internal and external to the company Theranos (Bijker, Hughes, & Pinch, 1987, pp. 17–50). Both social groups were pivotal in the development of the blood analyzer and how it was embedded in its social context. Internal groups such as CEO Elizabeth Holmes and the Theranos Board of Directors failed in their leadership, which resulted in an incomplete yet marketed product (Boni & Sammut, 2019). With the media as advertisement opportunities, pharmaceutical companies as investment opportunities, and regulatory agencies as development obstacles, these groups all directly influenced the development of the blood analyzer (Baird, 2019; Furlow, 2022).

Under SCOT, each social group has a relationship to the TBA which we will describe as the artifact (Bijker et al., 1987, pp. 17–50). Additionally, each social group bears perceived problems, and they see this artifact as a possible solution to their problems (Bijker et al., 1987, pp. 17–50). For example, Holmes and the Theranos Board of Directors perceived the TBA as a lucrative opportunity and media expansion platform (Boni & Sammut, 2019). From this, while the TBA inherited properties of increased media popularity, this artifact also inherited properties of rushed development and inaccurate data results, rather than properties of being regulatory compliant and safe for consumers (Das & Drolet, 2022). With Theranos rushing development and obscuring true testing results, the media grew fascinated with future goals and overall hype of the TBA, rather than gaining confidence due to true testing results. This artifact gained heightened technological momentum, which served as an intrinsic property leading to technological failure. While regulatory agencies would keep this artifact in check–slowing

development such that it would be safe and accurate for consumers–obscured and complete lack of communication with agencies such as the FDA and CLIA rendered their influence on this artifact to a minimum (Furlow, 2022).

As Theranos serves as a warning for future biotechnology companies regarding the consequences of rushed product development, new startups such as Drawbridge Health, Neoteryx, Tasso, Captainer, PanoHealth, HemoXis, and On the Spot are developing similar technology but with greater transparency and communication with regulatory agencies ("The Post-Theranos World," 2022). While these new companies are working to properly develop VAM, the proposed technology of the TBA, such companies must be mindful of TBA's SCOT theory for successful VAM development: to be unpersuaded by the momentum gained from the media and company-internal desires, and to develop devices for safe and accurate consumer use.

Research Question and Methods

My research question is: how has the Theranos blood analyzer, influenced by Elizabeth Holmes and the former climate of biotechnology startups, shaped the current healthcare and biotechnology industries? I plan to collect evidence through interviews and prior literature. I will conduct interviews with representatives of companies and agents who served a pivotal role in the development of the Theranos blood analyzer, such as Safeway and Walgreens (Bhattacharya, 2021), the Food and Drug Administration (FDA), and the Clinical Laboratory Improvement Amendments (CLIA). Although I have not yet reached out to such representatives, I believe they will provide the necessary information about my research topic through the perspective of these agencies. I will ask a variety of questions on Theranos' impact on their agency, and how they

plan to avoid a “future Theranos” from acting in the industry to get a better understanding of each agency’s perspective on the matter.

In terms of prior literature, I plan to research the dynamics played between various social groups and the blood analyzer. In particular, I will seek studies on current startups that plan to create a device similar to that of Theranos: how they perceive the development of Theranos’ blood analyzer and how their own, different development with foster success. My goal with this prior literature research is to fully develop and understand the interactions through the social construction of technology: in the context of Theranos’ blood analyzer, who are the stakeholders, what power and influence do such stakeholder yield on this device, and how did these interactions, dynamics, and relationships shape the design of Theranos’ blood analyzer.

Conclusion

The current ultrasound fHR monitors measure only a single fetal heart rate and are typically designed with the lower back obstructed. My technical project aims to deliver a working in-parallel transducer array that measures both amplitude and location of each fHR, developed with the verification of gel phantom to replicate the womb environment. My team's work will try to introduce a novel fetal heart rate monitor for multiple gestation pregnancies.

With my STS research, I aim to deliver a thorough and comprehensive social construction of Theranos’ blood analyzer, revealing the primary stakeholders and the influence they yield on this device through key interactions. This research will suggest a possible solution to ameliorate the flawed development of such biomedical devices. The effects of this research are to raise awareness of devices that failed due to development and how to anticipate or overcome these challenges or “red flags” for current and future biotechnology businesses and developers.

References

Adams, S. J., Yao, S., Mondal, P., Lim, H., Mendez, I., & Babyn, P. (2022). Sociodemographic and Geographic Disparities in Obstetrical Ultrasound Imaging Utilization: A Population-based Study. *Academic Radiology*, *29*(5), 650–662. https://doi.org/10.1016/j.acra.2021.07.012

Ayres-de-Campos, D., Stones, W., Theron, G., & the FIGO Safe Motherhood and Newborn Health Commitee. (2019). Affordable and low-maintenance obstetric devices. *International Journal of Gynecology & Obstetrics*, *146*(1), 25–28. https://doi.org/10.1002/ijgo.12838

Baird, G. S. (2019). If Theranos' Tests Had Actually Worked. *The Journal of Applied Laboratory Medicine*, *4*(1), 7–10. https://doi.org/10.1373/jalm.2019.029355

Bhattacharya, A. (2021, October 15). How Safeway and Walgreens fell for the Theranos pipe dream. Retrieved October 23, 2022, from Quartz website: https://qz.com/2074304/how-safeway-and-walgreens-fell-for-the-theranos-pipe-dream/

Bijker, W. E., Hughes, T. P., & Pinch, T. (1987). *The Social Construction of Technological Systems, anniversary edition: New Directions in the Sociology and History of Technology*. MIT Press.

Boni, A. A., & Sammut, S. M. (2019). "The Good, the Bad, the Ugly": Leadership Lessons From two Companies—Amgen and Theranos. *Journal of Commercial Biotechnology*, *24*(4), 67–73. https://doi.org/10.5912/jcb918

Das, R. K., & Drolet, B. C. (2022). Lessons from Theranos – Restructuring Biomedical Innovation. *Journal of Medical Systems*, *46*(5), 25. https://doi.org/10.1007/s10916-022-01813-3

Epidural: What It Is, Procedure, Risks & Side Effects. (2021, October 14). Retrieved October 24, 2022, from Cleveland Clinic website: https://my.clevelandclinic.org/health/treatments/21896-epidural

Euliano, T. Y., Darmanjian, S., Nguyen, M. T., Busowski, J. D., Euliano, N., & Gregg, A. R. (2017). Monitoring Fetal Heart Rate during Labor: A Comparison of Three Methods. *Journal of Pregnancy*, *2017*, 1–5. https://doi.org/10.1155/2017/8529816

Furlow, B. (2022). Theranos: The proof that public regulation matters. *The Lancet Oncology*, *23*(2), 204. https://doi.org/10.1016/S1470-2045(22)00024-9

Giles, W. B. (1998). 6 Doppler ultrasound in multiple pregnancies. *Baillière's Clinical Obstetrics and Gynaecology*, *12*(1), 77–89. https://doi.org/10.1016/S0950-3552(98)80041-2

Hamelmann, P., Kolen, A., Schmitt, L., Vullings, R., van Assen, H., Mischi, M., … Bergmans, J. (2016). Ultrasound transducer positioning aid for fetal heart rate monitoring. *2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 4105–4108. https://doi.org/10.1109/EMBC.2016.7591629

Hamelmann, P., Vullings, R., Kolen, A. F., Bergmans, J. W. M., van Laar, J. O. E. H., Tortoli, P., & Mischi, M. (2020). Doppler Ultrasound Technology for Fetal Heart Rate Monitoring: A Review. *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, *67*(2), 226–238. https://doi.org/10.1109/TUFFC.2019.2943626

Hill, G. D., Block, J. R., Tanem, J. B., & Frommelt, M. A. (2015). Disparities in the prenatal detection of critical congenital heart disease. *Prenatal Diagnosis*, *35*(9), 859–863. https://doi.org/10.1002/pd.4622

Kalikkot Thekkeveedu, R., Dankhara, N., Desai, J., Klar, A. L., & Patel, J. (2021). Outcomes of multiple gestation births compared to singleton: Analysis of multicenter KID database.

Maternal Health, Neonatology and Perinatology, *7*(1), 15. https://doi.org/10.1186/s40748-021-00135-5

Kollmann, C., Haar, G. ter, Doležal, L., Hennerici, M., Salvesen, K. Å., & Valentin, L. (2013). Ultraschall Emissionen: Thermische (TI) und mechanische (MI) Indizes. *Ultraschall in der Medizin - European Journal of Ultrasound*, *34*(05), 422–434. https://doi.org/10.1055/s-0033-1335843

Routh, H. F. (1996). Doppler ultrasound. *IEEE Engineering in Medicine and Biology Magazine*, *15*(6), 31–40. https://doi.org/10.1109/51.544510

The post-Theranos world. (2022). *Nature Biotechnology*, *40*(2), 139–139. https://doi.org/10.1038/s41587-022-01242-0

Waller, P. L., Ross, A., Hoskins, R. E., & Daling, J. R. (1993). Low birthweight in twins: Black and white differences. *Acta Geneticae Medicae Et Gemellologiae*, *42*(2), 159–169. https://doi.org/10.1017/s0001566000002051