Thesis Project Portfolio

Novel Bilirubin Quantification Method: Computational and *In Vitro* Validation

(Technical Report)

A Care and Duty Ethics Perspective on Pregnancy Exceptions in Life-Supporting Technology Policy

(STS Research Paper)

An Undergraduate Thesis

Presented to the Faculty of the School of Engineering and Applied Science

University of Virginia • Charlottesville, Virginia

In Fulfillment of the Requirements for the Degree

Bachelor of Science, School of Engineering

Kaitlyn Rose Hixson

Spring, 2024

Department of Biomedical Engineering

Table of Contents

Executive Summary

Technological developments have allowed for improved diagnosis and treatment of many conditions, including neonatal jaundice, which is condition characterized by yellow-tinged skin resulting from the accumulation of bilirubin, a biproduct of red blood cell breakdown. A non-invasive screening method, Transcutaneous Bilirubinometry (TcB), has been developed, however, TcB can overestimate the amount of bilirubin in infants with greater amounts of melanin (Olusanya et al., 2017). Incorrect measurement of jaundice leads to unnecessary or prolonged treatment for neonates with higher melanin concentrations. Thus, new bilirubin quantification methods are required to address this healthcare inequality and ensure accurate diagnostic ability. In addition to improvements and critical analysis of medical devices themselves, critical analysis needs to be brought to how medical devices are used to comply with Advance Directives in the context of pregnancy. To ensure protection and autonomy of vulnerable patients on life-support, healthcare decision-making tools, including Advance Directives (ADs), have been created. Autonomy is a cornerstone of clinical practice and has also been enshrined in legislation and judicial decisions, with notable exceptions for preserving life and protecting third parties (Kaplan, 2010). The state's interest in preserving life and protecting third parties has been used to justify statutes in ADs that nullify prospective withdrawal or withholding of care decisions when a patient is pregnant. Conflict between clinical practice guidelines requiring the upholding of ADs and legal requirements nullifying AD decisions to withhold or withdrawal of life-supporting devices during pregnancy presents questions concerning the ethicality of AD pregnancy exceptions that needs to be discussed.

To address the healthcare disparity that current TcB devices present, a physiologically relevant computational and *in vitro* physical model will be created to determine the viability of a

novel skin-tone inclusive bilirubin measurement method. A prior Capstone demonstrated proof-of-concept for a method of quantification using the known photoconversion property of bilirubin. As bilirubin is converted into lumirubin under 460 nm light shining on a small area, the decreasing absorbance measurements over time were used to calculate initial bilirubin concentration. The prior group demonstrated effectiveness in cuvettes, representing an oversimplified model of bilirubin accumulation, but a more complex model is necessary for further validation of the measurement method (Yurish, 2023). In this technical project, a more detailed computational and *in vitro* physical model were created to further determine viability of this novel bilirubin quantification method. A diffusion-reaction partial differential equation was used to develop a time-dependent analytical model for neonatal bilirubin concentration with optimization and validation of model parameters using an *in vitro* experimental model. The *in vitro* flow dialysis model contained bilirubin solution dialyzing into a hydrophobic layer, mimicking bilirubin diffusion into tissue and providing a more robust proof-of-concept for this method of quantifying bilirubin.

With the development of new life-supporting technologies that can mechanically provide necessary vital functions, people can now be kept alive in a coma or permanent vegetative state, which has led to the issue of preserving patient autonomy when they are unable to advocate for themselves. One of the most widely used tools for establishing prospective healthcare treatment decisions is the AD, which includes specific instructions pre-authorized by the patient and the designation of a healthcare decision-making proxy. However, in 27 states there are statutes in AD legislation that invalidate an AD if a patient is pregnant (*Guide to State Laws On Advance Directives and Pregnancy*, n.d.). AD pregnancy exceptions prevent the withholding or withdrawing of life-supporting care from a pregnant patient regardless of the patient's previously

expressed wishes, helping to ensure the fetus is carried to term. Pregnancy exceptions demonstrate the states' interest in protecting human life, but they can also interfere with ethical clinical practice and care that aligns with the patient's wishes or best interests, which prompts the question: How have duty and care ethics shaped the regulation of life-supporting devices during pregnancy and what are the ethical implications of policies that regulate this technology? Using duty and care ethics frameworks, the interplay between clinical practice and state legislation regarding pregnant patients' use of life-supporting technology is discussed.

Together, these projects emphasize the importance of the four pillars of clinical ethics, including justice, beneficence, non-maleficence, and autonomy, in both clinical practice and legislation. Through the validation of a novel, skin-tone inclusive method for measuring bilirubin, the pillars of justice, beneficence, and non-maleficence are promoted with the validation of a more accurate bilirubin quantification method to improve clinical decision-making. In the analysis of AD pregnancy exceptions from the perspective of the pillars of clinical ethics, clinical practice is considered in cases where a patient's AD is invalidated due to pregnancy. Through this lens, prioritizing the state's interest in preserving life over the patient's bodily autonomy through AD pregnancy exceptions violates all of the pillars of clinical ethics and can place doctors in complex and ethically compromising situations. Thus, to treat patients to the highest standard, the pillars of clinical ethics must be exemplified and adhered to in both medical devices themselves and how they are used.

Works Cited

Guide to State Laws On Advance Directives and Pregnancy: Charts and Links. (n.d.). Do It Yourself Legal Forms - FindLaw. Retrieved April 4, 2024, from https://www.findlaw.com/forms/resources/living-will/guide-to-state-laws-on-advance-directives-and-pregnancy-charts-and-links-2.html

Kaplan, M. (2010). *"A Special Class of Persons": Pregnant Women's Right To Refuse Mdical Treatment After Gonzales V. Carhart*. *13*(1), 145–206.

Olusanya, B. O., Mabogunje, C. A., Imosemi, D. O., & Emokpae, A. A. (2017). Transcutaneous bilirubin nomograms in African neonates. *PLoS ONE*, *12*(2), Article 2. https://doi.org/10.1371/journal.pone.0172058

Yurish, C. (2023). *Design of a Skin-Tone Inclusive Technique for the Non-Invasive, Transcutaneous Measurement of Bilirubin; Healthcare Providers, Federal Agencies, and the Media Change in Trust Due to Bias Found in Pulse Oximeters.* University of Virginia, School of Engineering and Applied Science, BS (Bachelor of Science), 2023. Retrieved from https://doi.org/10.18130/f1bz-5985