Development of Hepatic Vasculature Models for Preoperative Planning
(Technical Report)

Analysis of Racial Disparities in the Diagnosis and Treatment of Liver Cancer in the U.S.
(STS Research Report)

A Thesis Prospectus Submitted to the

Faculty of the School of Engineering and Applied Science
University of Virginia • Charlottesville, Virginia

In Partial Fulfillment of the Requirements of the Degree
Bachelor of Science, School of Engineering

Kara Tung

Fall 2023

Technical Project Team Members: Sophia Godfrey & Radha Patel

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

Signature _*Kara Tung*_________________________________ Date _11/19/2023__
Kara Tung

Technical Advisors
John F. Angle, M.D., Department of Interventional Radiology
Timothy Allen, Ph. D., Department of Biomedical Engineering

STS Advisor
Richard D. Jacques, Ph.D., Department of Engineering & Society

Introduction

The liver is the largest internal organ. It is responsible for digesting fat, storing glycogen (one of the body's main energy resources), and filtering substances from the blood into urine and stool (*What Is Liver Cancer?*, 2022). Liver cancer is the third leading cause of cancer-related deaths worldwide. It has been estimated that cases may increase by more than 55% within the next twenty years (*What Is Liver Cancer?*, 2022). If the cancer is caught early enough, the only current, curable treatment options are a partial hepatectomy or a liver transplant (*Treatment of Liver Cancer, by Stage*, n.d.). All other treatments may reduce symptoms and lengthen the survival rate.

Arterial embolization is a treatment option often used for tumors that are too large to be treated with ablation therapy or tumors that cannot be surgically removed (*Embolization Therapy for Liver Cancer*, n.d.). During the procedure, embolization agents are delivered to block the vessels that feed nutrient-rich blood to tumors. Patients who undergo hepatic arterial embolization have shown survival rates of almost 30% for five years after treatment (Lee et al., 2012). In comparison, liver cancer that goes untreated or undiagnosed until later stages can spread to other parts of the body, resulting in a 5-year survival rate of 3% (*Liver Cancer Survival Rates | Cancer of the Liver Survival Rates*, n.d.).

3D models of human anatomy are commonly used in medical education and for planning surgery. These models range from hard, plastic models of bone to malleable, realistic models of the kidney and liver (Kraft et al., 2021). For complicated cases, surgeons often rely on 3D reconstructions to visualize the vessels of the liver. Specifically, models have been developed for liver resection or transplantation procedures (Valls-Esteve et al., 2023). Previously, angiography models of human vascular anatomy have been mostly silicone approximations of arterial anatomy and only involve modeling large or medium-sized vessels. However, modern 3D printers now allow the creation of a model of liver vasculature with surrounding soft tissue based on real human CT angiography data. Additionally, these models show the potential to demonstrate the physiologic blood flow to allow testing of arterial embolization agents.

Technical Discussion

Arterial embolization is a minimally invasive procedure that utilizes the insertion of a catheter. Because it depends on real-time medical imaging to guide the process, it can be one of the most technically difficult procedures (Bagla & Isaacson, 2016). Ultrasound and CT imaging do not give a detailed visualization of the vessel network, so surgeons must rely on fluoroscopy and contrast agents throughout the surgery to determine the location of the catheter head.

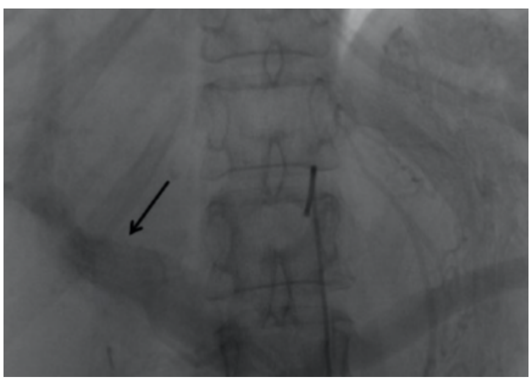
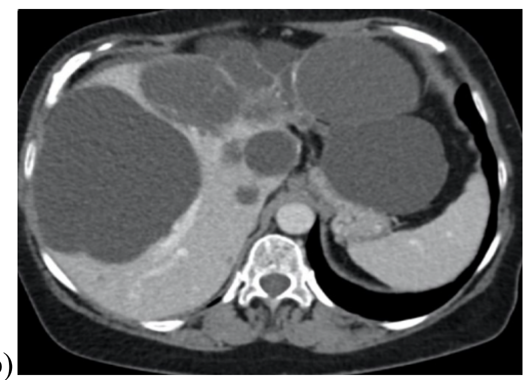
a)  b) 

Figure 1: a) CT portography of the hepatic artery b) CT image of the liver cross-section (Coussy et al., 2022)

As shown in Figure 1, the hepatic artery is not clearly defined in any of the CT images. These images offer enough anatomical detail to guide the surgeons to the general location within the body, but the imaging lacks the necessary level of detail to accurately navigate the catheter within the intricate vessel architecture. Additionally, the anatomy of the vasculature within the liver and around a tumor already presents a challenge to navigate.

From shadowing in the Interventional Radiology (IR) Department at UVA Health, at the beginning of October 2023, my Capstone team was able to observe the slow and steady process of the surgeons carefully maneuvering the catheter and surgical instruments through the patient to locate the target artery. Hepatic arterial embolization can take up to three hours (*Patients & Families | UW Health*, n.d.). During the procedure my Capstone team shadowed, the surgeons were having difficulty finding the right angle to guide the catheter through the body. Because of the lack of detail that the imaging provided, it took them additional time to confirm if they were located in the right artery or vessel.

The goal of this project is to develop a 3D flow model of liver vasculature for arterial embolization testing. The project aims to expand the use of 3D-printed organ models as medical teaching tools and communication tools used in clinical settings. While 3D printing has been implemented in a variety of applications for preoperative planning and anatomical teaching, models representing the minute details of the vasculature are limited due to current 3D printing processes and machines. My Capstone team will be exploring how well resin 3D printing can capture the minute details of the hepatic vascular system at a 2 mm scale. As mentioned above, most angiography models have explored large to medium-sized vessels; we will be pushing the boundaries of the scale to model vessels branching from the hepatic tree with diameters ranging from 5 mm to 2 mm. Our team has defined three specific objectives for this project: 1) extract the hepatic vascular tree from real patient CT images, 2) 3D print the vascular tree from a rendering of CT data with attention to potential inflow and outflow, and 3) create a model for the physiologic flow within the liver.

Our technical advisor is Dr. John Angle, an interventional radiologist at the UVA hospital. He will provide ten CT scans of patients' liver vasculature, from which my Capstone team will convert the CT data into a usable format to develop a model using CAD software for 3D resin printing. My Capstone team will be utilizing Picture Archiving and Communication System (PACS) software and syngo.via software, which will de-identify patient data prior to saving and exporting files. PACS software can convert the files to DICOM format, which can be uploaded into a 3D slicer and CAD software (i.e., Rhino Medical). The goal is to finish 3D printing and prototyping by the beginning of December. The following months in the Spring semester will be dedicated to modeling the physiologic flow in our 3D model.

For the 3D printing process, we plan to experiment with Silicone 40A, Elastic 50A, and Flex 80A resins from Formlabs© to determine what resin type will allow for the most defined vascular structures while attempting to model vascular mechanics. After many iterations of printing hollow vessel structures, we will hopefully obtain a working prototype to be tested with blood analogs and radiographic contrast. We will do this by feeding a catheter into our model and measuring the flow with immunofluorescent contrast materials to compare to existing data. Our advisor plans to provide us with a commercially available pump to simulate the blood flow. We aim to develop a product that will allow physicians to practice guiding a catheter through an intricate model that is to scale and with specific attention to flow that will allow for the testing of embolization agents.

STS Discussion

Arterial embolization is a common procedure that is used to manage liver metastases. It has a high success rate range of 80-97% and is less invasive than open surgery (Virdis et al., 2019). The results have led to long-term survival rates of 5-10 years of liver cancer, even at Stage IV (Lee et al., 2012). My STS research will specifically focus on hepatocellular carcinoma

(HCC), the most common type of liver cancer. There are disproportionate rates of treatments and diagnoses of HCC, with the highest rates among racial minority groups, specifically Hispanic and Black populations in the United States (Ajayi et al., 2020).

While data is limited on the factors and determinants of these disparities, there is an evident correlation that points to under-surveillance and underutilized treatments among these patients (Ajayi et al., 2020). Because of this, Black and Hispanic individuals are often diagnosed with liver cancer at a more advanced stage compared to white individuals. In addition, metabolic diseases, such as diabetes and obesity, are major risk factors for liver cancer, often progressing to HCC, especially when these diseases are not well-managed or managed at all. The highest prevalence of obesity in the U.S. is seen among 50% of Black adults and 45% of Hispanic adults (Vidal et al., 2022). According to the American Association for Cancer Research (AACR), even among focus groups, there is a significant lack of awareness that HCC disproportionally affects minority groups, especially Black adults (Licciulli, 2021). Research on these upstream factors is crucial to implement preventative measures in order to address these disparities among minority populations.

Although minority populations have the highest rates of infection, they still have lower rates of treatment (Licciulli, 2021). Minority patients are less likely to receive guideline-recommended treatments for liver cancer, such as surgical resection, liver transplantation, or minimally invasive procedures like arterial embolization (Singh & Singh, 2020). During a multivariable analysis, there was an association found between all-cause mortality of HCC and the lack of guideline treatments in addition to treatment locations in hospitals that do not have residency training (Harlan et al., 2015). All-cause mortality refers to the overall death rate without distinguishing between the specific causes. A range of factors, including disparities in general healthcare access, limited access to specialized facilities, and socioeconomic status, contribute to this. The analysis implies that facilities without residency training programs may lack the specialized expertise and resources to perform newer, less invasive procedures, such as arterial embolization, thereby further exacerbating the treatment disparities faced by minority populations.

My STS research focuses on analyzing the racial disparities in the diagnosis and treatment of liver cancer, while my technical research works towards advancing the knowledge and skill set required to perform arterial embolization as a treatment for liver cancer.

The primary motivation for my Capstone project is the idea that viable learning tools make medical residents and physicians better caregivers. Our 3D model can also be utilized as a learning and communication tool with patients. Often when patients have reservations about surgeries and procedures, it is because of their lack of knowledge and understanding of the procedure. A 3D model can be utilized in this situation to demonstrate to patients exactly what they should expect, which will help facilitate trust and communication between the physician and the patient. By providing a visual of the procedure, this goal will also aim to improve communication with patients who do not speak English as their primary language. Our broader goal and implication of our Capstone project is to help bridge gaps of communication and trust between patients and their physicians.

Conclusion

Liver cancer poses a threat to public health, with the potential for a substantial increase in cases over the next two decades. Early detection and treatment are key to improving survival rates, and while partial hepatectomy and liver transplant are the curative options, arterial embolization presents a valuable alternative for certain cases. However, the technical complexities of arterial embolization, exacerbated by the limitations of current imaging technologies, make it a challenging procedure for healthcare providers.

My Capstone project is focused on creating a 3D flow model of the liver's vasculature for arterial embolization testing, offering a potential aid to these challenges. By utilizing advanced 3D printing technology and real patient CT data, this project seeks to enhance the precision and effectiveness of arterial embolization by providing a detailed, anatomically accurate model for preoperative planning and procedural practice.

Furthermore, the intersection of the technical and STS aspects of this project regards the existing medical care of liver cancer. By addressing the racial disparities in the diagnosis and treatment of liver cancer, the STS research component adds a crucial dimension to the project's goals. Understanding and mitigating these disparities, particularly in the context of treatments like arterial embolization, is essential for promoting equitable healthcare outcomes. Of particular importance is the development of 3D models as educational and communication tools that have the potential to enhance patient-physician communication and trust, ultimately fostering better healthcare experiences and outcomes.

In summary, this project highlights the valuable role that cutting-edge technology, interdisciplinary research, and innovation can play in the enhancement of healthcare, through improved patient care, increased equity, and better medical education and communication. The fusion of technical expertise and societal understanding embodied in this endeavor exemplifies the dynamic and multifaceted nature of modern healthcare advancements.

Resources

Ajayi, F., Jan, J., Singal, A. G., & Rich, N. E. (2020). Racial and Sex Disparities in Hepatocellular Carcinoma in the USA. *Current Hepatology Reports*, *19*(4), 462–469. https://doi.org/10.1007/s11901-020-00554-6

Bagla, S., & Isaacson, A. J. (2016). Tips and Tricks for Difficult Prostatic Artery Embolization. *Seminars in Interventional Radiology*, *33*(3), 236–239. https://doi.org/10.1055/s-0036-1586145

Coussy, A., Jambon, E., Le Bras, Y., Combe, C., Chiche, L., Grenier, N., & Marcelin, C. (2022). The Safety and Efficacy of Hepatic Transarterial Embolization Using Microspheres and Microcoils in Patients with Symptomatic Polycystic Liver Disease. *Journal of Personalized Medicine*, *12*(10), Article 10. https://doi.org/10.3390/jpm12101624

Embolization Therapy for Liver Cancer. (n.d.). Retrieved September 26, 2023, from https://www.cancer.org/cancer/types/liver-cancer/treating/embolization-therapy.html

Harlan, L. C., Parsons, H. M., Wiggins, C. L., Stevens, J. L., & Patt, Y. Z. (2015). Treatment of hepatocellular carcinoma in the community: Disparities in standard therapy. *Liver Cancer*, *4*(1), 70–83. https://doi.org/10.1159/000367729

Kraft, V., Schumann, C., Salzmann, D., Nopper, H., Lück, T., Weyhe, D., & Schenk, A. (2021). Towards realistic organ models for 3D printing and visualization. *Current Directions in Biomedical Engineering*, *7*(1), 166–170. https://doi.org/10.1515/cdbme-2021-1036

Lee, E., Leon Pachter, H., & Sarpel, U. (2012). Hepatic arterial embolization for the treatment of metastatic neuroendocrine tumors. *International Journal of Hepatology*, *2012*, 471203. https://doi.org/10.1155/2012/471203

Licciulli, S. (2021, October 18). Reflecting on the Racial Disparities in Liver Cancer. *American*

Association for Cancer Research (AACR). https://www.aacr.org/blog/2021/10/18/reflecting-on-the-racial-disparities-in-liver-cancer/

Liver Cancer Survival Rates | Cancer of the Liver Survival Rates. (n.d.). Retrieved October 13, 2023, from https://www.cancer.org/cancer/types/liver-cancer/detection-diagnosis-staging/survival-rates.html

Patients & Families | UW Health. (n.d.). Retrieved October 21, 2023, from https://patient.uwhealth.org/healthfacts/5763

Singh, S. K., & Singh, R. (2020). Liver cancer incidence and mortality: Disparities based on age, ethnicity, health and nutrition, molecular factors, and geography. *Cancer Health Disparities*, *4*, e1–e10.

Treatment of Liver Cancer, by Stage. (n.d.). Retrieved October 21, 2023, from https://www.cancer.org/cancer/types/liver-cancer/treating/by-stage.html

Valls-Esteve, A., Tejo-Otero, A., Lustig-Gainza, P., Buj-Corral, I., Fenollosa-Artés, F., Rubio-Palau, J., Barber-Martinez de la Torre, I., Munuera, J., Fondevila, C., & Krauel, L. (2023). Patient-Specific 3D Printed Soft Models for Liver Surgical Planning and Hands-On Training. *Gels*, *9*(4), 339. https://doi.org/10.3390/gels9040339

Vidal, A. C., Moylan, C. A., Wilder, J., Grant, D. J., Murphy, S. K., & Hoyo, C. (2022). Racial disparities in liver cancer: Evidence for a role of environmental contaminants and the epigenome. *Frontiers in Oncology*, *12*. https://www.frontiersin.org/articles/10.3389/fonc.2022.959852

Virdis, F., Reccia, I., Di Saverio, S., Tugnoli, G., Kwan, S. H., Kumar, J., Atzeni, J., & Podda, M. (2019). Clinical outcomes of primary arterial embolization in severe hepatic trauma: A systematic review. *Diagnostic and Interventional Imaging*, *100*(2), 65–75. https://doi.org/10.1016/j.diii.2018.10.004

What Is Liver Cancer? - NCI (nciglobal,ncienterprise). (2022, May 19). [pdqCancerInfoSummary]. https://www.cancer.gov/types/liver/what-is-liver-cancer