Automatic Segmentation and 3D Reconstruction of the Inner Ear Vasculature from Histology Slides

Paper Seminar Report

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Project Summary

Histology slides of the inner ear are critical to understanding the pathophysiology of various pathologies in otolaryngology. However, despite the importance of analyzing histology slides, most researchers still rely on manual methods for analysis of structures within the inner ear. These methods can be time-consuming and are subject to poor inter rater reliability. Additionally, these manual segmentations typically are not able to capture information in 3D, which can reveal additional critical information about the pathophysiology. This project aims to create software that can automatically extract critical features such as vasculature from histology and reconstruct these segmentations to create 3D models.

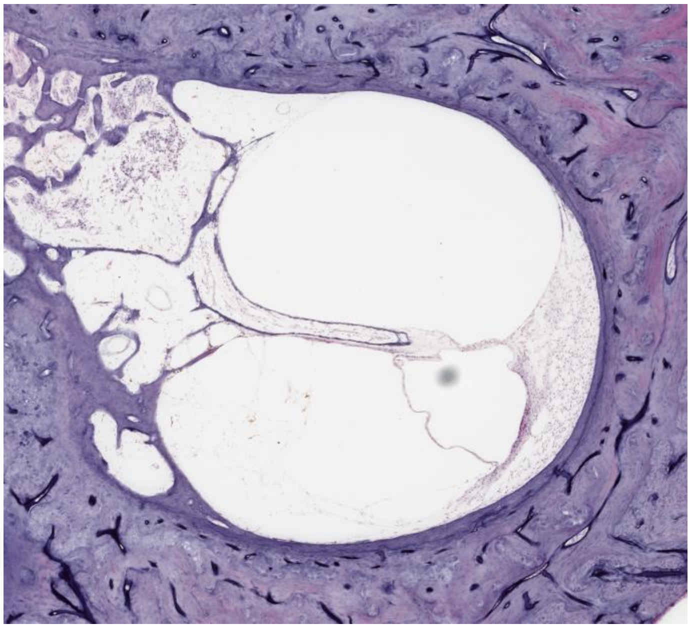

Figure 1: Example of histology section of the inner ear

Paper

"Spatial analysis of histology in 3D: quantification and visualization of organ and tumor level tissue environment" was chosen for specifically as an example of 3D reconstruction of histology, a task that this project hopes to replicate [1]. This paper primarily focuses on performing 3D reconstruction of organ(prostate) slides with tumors in order to better understand volumetric data relating to tumors. The paper outlines useful alignment/registration techniques as well as methods to extract volumetric data that are relevant this project. Furthermore, the paper proposes a generalized pipeline for 3D reconstruction of histology slides.

Summary and Key Results

The authors of this paper were able to successfully align and reconstruct the prostate gland from histology sections across 6 mice with tumors. An overview of the results is shown below in Figure 2. Using manual segmentation of the tumor across the slices, the authors were able to then analyze tumors for various volumetric features such as volume, surface area, sphericity, etc. The authors applied PCA to these features to successfully cluster these cancers and make predictions about growth patterns in prostate tumors.

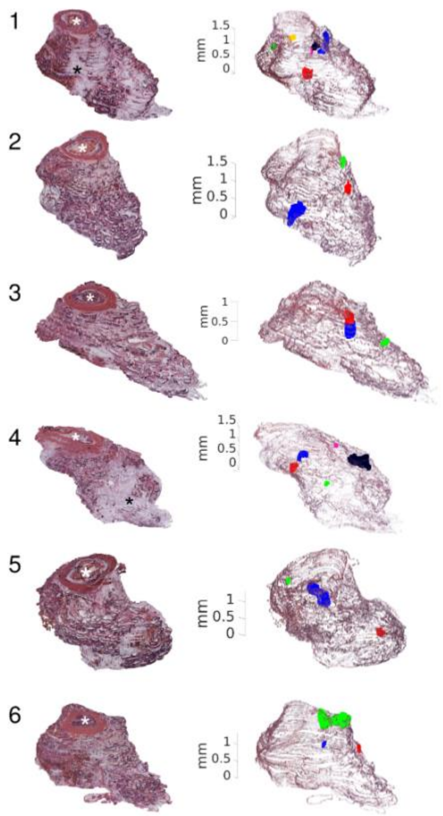

Figure 2. 3D reconstruction of prostate gland from histology slices with tumors highlighted in various colors.

Background

The authors of this paper based their work primarily on their own previous research [2]. In their prior work, the authors compare various techniques to align and reconstruct histology slides. They also note the importance of study histological section in 3D to better characterize tumor pattern growth. In this paper, they propose an improvement to their method that uses an Elastic Stack Alignment with Bayesian optimization based hyper-parameter tuning.

Method Overview

An outline of the proposed method to reconstruct the prostate gland in 3D is shown below in Figure 3. The authors began by manually labelling tumor region of interests across histology sections.

Tissue Alignment

The authors used the Elastic Alignment features in Image J to align each of the slices of the specimen. Prior to inputting each image, the authors first down sampled the original image to extract the border of each slice. The authors then used this mask to remove small artifacts from the background. The authors then down sampled the original image to ½ of the original size and performed registration on these images. The elastic alignment feature in ImageJ has numerous hyperparameters. To optimize the registration the authors proposed Bayesian optimization based warm start to find the parameters that would result in the lowest error as defined by

$$E_{reg} = \frac{\sum_{i=0}^{M}\sum_{j=0}^{N}|A_{ij}|(I_{ij}^{S} - I_{ij}^{S+1})^2}{\sum_{i=0}^{M}\sum_{j=0}^{N}|A_{ij}|},$$

where

$$A = I^{(S+1)} * L.$$

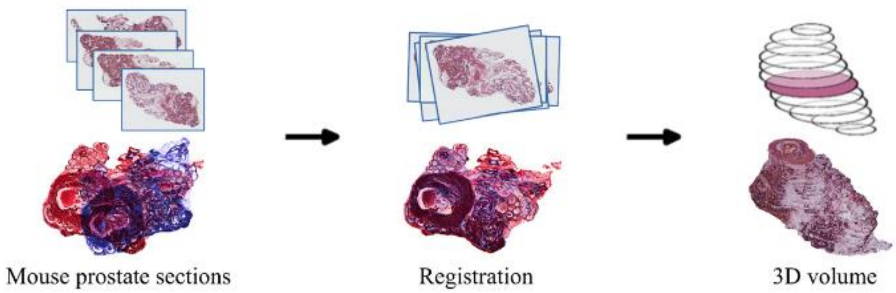

Figure 3. Overview of 3D reconstruction of prostate from histology sections.

3D Reconstruction and Analysis

Once the authors had registered each of the section, the authors used Matlab to visualize their representations. The features of the 3D reconstructed ROI were extracted using a combination of matlab and python. Such feautres included volume, surface area, centricity, size of bounding box, etc. The authors then primarily used PCA to cluster these features and capture information about tumor growth.

Results

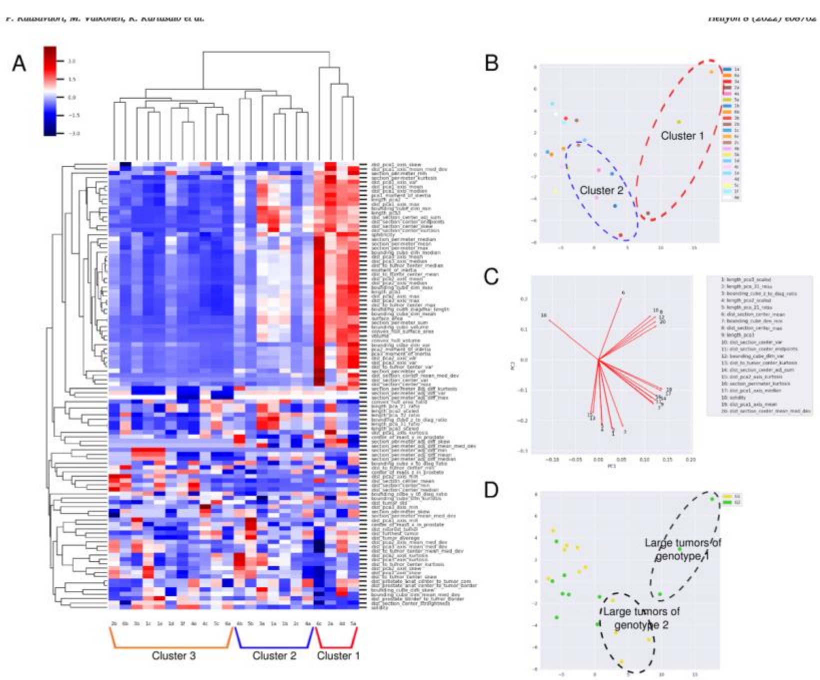

Figure 4. Results of clustering volumetric information of tumors from 3D reconstruction

The authors demonstrate that, through volumetric analysis, they are able generate clinically relevant information. As shown in figure 4, the authors identified 3 broad clusters from performing PCA that enables them to subdivide and further understand tumor morphology. The authors argue that stratify tumors this way could enable future work to better predict outcomes based on volumetric analysis. Additionally, the authors were able to extract clinically relevant data points such as distance to the edge of the prostate and average location within the prostate; these features could also play a role in predicting growth patterns for certain tumors.

Paper Critiques

Pros

The pipeline outlined in this paper successfully accomplishes the goal of being able to visualize and assess tumor in 3D based on the histology slides. The analysis used by the authors shows the advantages of using 3D analysis techniques compared to solely using 2D metrics especially with regards to predicting growth patterns and studying cancer morphology. This paper clearly is a good starting point for future work in the field of 3D histology.

Cons

Perhaps the biggest issue with this paper is the size and type of the dataset. The authors studied 6 mice prostrates that encompassed 22 tumors. With such a small dataset, the author's results proposed sections may not be generalizable to the rest of the population. Also, this work was done with mice prostate sections which has slightly different anatomy compared to human ones. An additional limitation of the study is the reliance on manual segmentation methods for tumor identifications. The authors do not verify the accuracy or reliability of these segmentation techniques.

Next Steps

The authors acknowledge that this paper is just a starting point: they understand that adding more data would enable them to give more clinically relevant data. The authors could also consider adding in machine learning techniques to segment out the tumor region of interest.

Implementation in Current Project

The pipeline for 3D reconstruction outlined in the paper could serve as template for this project to generate 3D reconstructions of the inner ear histology. While the analysis used in this paper for volume assessment may not be relevant for quantifying features in inner ear histology, it presents an interesting idea to use PCA to do statistical shape modeling with 3D reconstruction perhaps across multiple specimens.

References:

1. Ruusuvuori P, Valkonen M, Kartasalo K, Valkonen M, Visakorpi T, Nykter M, Latonen L. Spatial analysis of histology in 3D: quantification and visualization of organ and tumor level tissue environment. Heliyon. 2022 Jan 14;8(1):e08762. doi:10.1016/j.heliyon.2022.e08762. PMID: 35128089; PMCID: PMC8800033.
2. K. Kartasalo, L. Latonen, J. Vihinen, T. Visakorpi, M. Nykter, P. Ruusuvuori, Comparative analysis of tissue reconstruction algorithms for 3D histology, Bioinformatics 34 (17) (2018) 3013–3021.