**SEMINAR REPORT**

**SEMINAR 6**

**Speaker:**  
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**Topic:**  
*Statistical Modeling of Topological Features in Medical Imaging: Enhancing Prognostic Precision and Interpretation*

**Abstract**

Dr. Chul Moon's seminar presented innovative statistical methods for analyzing tumor morphology in medical images to predict patient survival and understand tumor behavior. He introduced *topological features* obtained through persistent homology to analyze tumor shapes across pathology and radiology images, emphasizing their ability to capture shape patterns invariant to scale-preserving transformations. Using these features, a novel *functional spatial Cox proportional hazards model* was developed. This model incorporates topological features as functional predictors linked with spatial locations, offering interpretable relationships between tumor morphology and survival risks.

**Analytical Tools from Topology: Homology**

* **Homology** analyzes the structure of a topological space XXX by identifying its *k-dimensional holes* (topological features). These include:
  + **Zero-dimensional** holes: Connected components
  + **One-dimensional** holes: Loops
  + **Two-dimensional** holes: Voids
* **Betti Numbers** (rank of H(X)H(X)H(X)) provide a count of k-dimensional holes, offering a quantitative way to assess tumor structure complexity.

**Prediction Using Cross-Validation**

Using leave-one-out cross-validation (LOOCV), risk scores were computed for the CoxPH and Functional CoxPH (FCoxPH) models. The models classified patients into high- and low-risk groups, with statistically significant separation (p-values of 6 × 10^-5 for CoxPH and 1 × 10^-12 for FCoxPH). The Kaplan-Meier survival plots confirmed improved prognostic accuracy for the FCoxPH model.

**Representing Image Data as Complexes**

To compute homology on medical image data, images are represented as *cubical complexes*. This involves converting grayscale images to binary images and then organizing them into a structure that approximates a topological space, capturing fundamental shape information.

**Persistent Homology**

Persistent homology captures homology across various threshold levels, called *filtrations*. By analyzing the "birth" and "death" of topological features, persistent diagrams are created, which map these changes across dimensions. This approach allows for a robust representation of tumor shape features across varying scales.

**Data of Interest: AI-Processed Medical Images**

This study primarily uses multi-class medical images, such as binary (tumor vs. non-tumor) and ternary (tumor, normal, and empty regions) images. Techniques like the *Signed Euclidean Distance Transform for Ternary Images (SEDT-3)* were proposed for converting complex multi-class images into functional data representations for analysis.

**Topological Data Analysis of Binary Images**

The persistent homology results for binary images reveal two primary types of features:

1. **Dimension Zero Features**: Analyze size and distribution of tumors.
2. **Dimension One Features**: Evaluate shapes of tumor regions, identifying ring and broken-ring formations that correspond to tumor morphology.

**Functional Representation of Persistence Diagrams**

To make persistent diagrams usable in data analysis, they are transformed into *persistence functions*, allowing for representation in a functional space that facilitates modeling and prediction.

**Case Study: Lung Adenocarcinoma**

Using pathology images from lung adenocarcinoma patients, the study demonstrated how FCoxPH models can integrate clinical variables with topological shape features. These images, segmented by deep convolutional neural networks, are processed to highlight tumor, normal, and empty regions, allowing for more refined hazard modeling.

**Cox Proportional-Hazards Model (FCoxPH)**

The FCoxPH model extends the traditional CoxPH by incorporating functional predictors derived from the topological features. Functional PCA (FPCA) is used to reduce the dimensionality of these functional data predictors, ensuring computational efficiency.

**Glioblastoma Multiforme Case Study**

Analysis of brain tumor images for Glioblastoma Multiforme (GBM) reveals patterns associated with survival risks, incorporating not only tumor shape features but also their spatial information within brain lobes. An indicator function adds locational context to the FCoxPH model, improving prognostic power.

**Dimension Reduction Using Regularization**

The L1 penalty is applied to the survival models for dimension reduction. The final models, FCoxPH and CoxPH-Radiomic, include clinical variables and topological features, showing that topological shape features alone improve survival predictions without the need for radiomic features.

**Prediction Using Cross-Validation**

The LOOCV results demonstrate the prognostic capabilities of the models. For example, the FCoxPH model achieves a p-value of 4 × 10^-7, indicating a significant separation between high- and low-risk patient groups, further validated by Kaplan-Meier plots.

**Conclusion and Future Directions**

The seminar concluded with the finding that topological shape features have significant prognostic value in survival modeling. These features successfully capture tumor aggressiveness and align with clinical insights. Future research will focus on:

* Extending topological analysis to multi-class pathology images.
* Investigating associations between topological features and genetic markers or mutations.