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PhD Thesis Title: Representation Methods for Imaging-based Multi-level Cancer Heterogeneity: Towards Virtual Biopsy and Prognostic Subtyping

The field of oncology continues to face significant challenges in characterizing intra-tumor heterogeneity effectively and exhaustively. Despite years of research and producing a large amount of multi-view data, clinically relevant and statistically sound models for understanding the disease still need to be discovered. Traditional methods such as omics profiling and biopsies have limitations in fully predicting the tumor's clonal dynamics trajectory. As a result, the under-representation of tumor information has hindered the translation of precision medicine techniques into clinical practice.

To address these challenges, this thesis proposes the creation of a more exhaustive representation of the tumor, known as a virtual biopsy, and using this representation to aid clinical decision-making and prognostic cancer subtyping. The contributions of this thesis are two-fold: The first part focuses on developing a virtual biopsy framework for characterizing intra-lesion tumor radiological heterogeneity, with applications in the context of Colorectal cancer. The second part explores and exploits representation methods for intra-patient radiological heterogeneity and proposes approaches tested and discussed with regard to two multi-lesion cancers: Hodgkin Lymphoma and Prostate cancer. Real-world applications for cancer subtyping and prognostic profiling are employed using supervised, unsupervised, and weakly supervised learning.

The difficulty in finding effective imaging biomarkers for therapeutic purposes necessitates the collaboration of different fields, such as medicine, mathematics, geometry, and computer science. This collaboration would lead to a mathematically sound model capable of capturing an image's exhaustive and representative textural and structural features for targeted virtual biopsy purposes. Ultimately, it would improve and go beyond the current radiomic framework to draw prognostic inferences that can be used in clinics.

This thesis supports the vision of collaboration between disciplines leading to new ways of modeling, eventually slowing down tumor growth and preventing treatment resistance. The proposed methods and frameworks have significant potential to advance the field of oncology and pave the way for more effective and personalized cancer treatment.