## Spatio-temporal Prediction of Tumor Evolution with uncertainty quantification using evidential machine learning

Radiotherapy is one of the standard treatments for tumors. However, nearly 20% of patients do not respond to it, leading to suboptimal outcomes. To better understand the mechanisms of resistance and predict treatment response before administration, extensive research is being conducted in medicine.

This thesis aims to develop new machine learning (ML) methods to optimize radiotherapy and patient monitoring by leveraging multimodal and longitudinal data. The objective is two-fold:

- Predict tumor evolution at the pixel or voxel level based on longitudinal multimodal datasets.
- Assess therapeutic response at the patient level to adjust treatment strategies during the protocol.

These predictive models rely on the analysis of diverse data types, including medical images (MRI, PET, etc.), biomarkers, and clinical parameters collected at different follow-up time points. A key challenge for their clinical application lies in managing uncertainties. Although multimodal data fusion and uncertainty quantification have been explored in medical imaging [1, 2], pixel-wise or voxel-wise prediction of tumor evolution remains under-investigated [3, 4, 5].

Evidential ML is an approach to ML based on the theory of belief functions, which provides a robust framework to simultaneously model prediction uncertainties and fuse heterogeneous data [6]-[9]. Recently, it has been to medical image segmentation [10, 11]. This thesis will therefore explore fusion methods based on this theory to build robust predictive models that account for uncertainty quantification in predictions, thereby supporting clinical decisions.

The expected outcomes will contribute to more personalized medicine, improving treatment effectiveness while reducing associated risks. The validation of the proposed system will be carried out in collaboration with the Hospital Center of Rouen.

This PhD thesis will be supervised by Professor Thierry Denoeux (Université de Technologie de Compiègne) and Professor Su Ruan (University of Rouen Normandy) as part of a collaboration between the two laboratories Heudiasyc and AIMS.

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## Abstract in Chinese:

放射治疗仍是核心治疗方式,但约有 20% 的患者因治疗症状而出现肿瘤恢复。本博士论文旨在通过整合多模态纵向数据(包括 MRI、PET 等医学影像、生物标志物和临床参数)开发一种新型机器学习 (ML) 框架,以优化放射治疗计划和实时患者监测。研究的核心挑战是解决临床数据的不确定性,从而有效地预测和做出临床决策。尽管先前的研究已经探索了多模态数据融合和不确定性,但在空间分辨率(像素/体素级别)上的肿瘤预测仍未得到充分探索。为了填补这一空白,本研究使用基于证据的机器学习 (evidential ML) 借鉴其在医学图像分割方面的成功经验,构建一个稳健且可解释的模型,用于预测肿瘤治疗进展和对治疗的反应。通过提供不确定性认知的个性化分析,提出的模型旨在为临床医生提供可操作的决策工具,以支持治疗计划的动态调整,从而促进精准肿瘤学的发展并提高成功率。