## Deep Learning in B-mode Ultrasound Imaging: from Discriminative Analysis to Generative Models

B-mode ultrasound imaging stands as a key diagnostic tool due to its safety, cost-effectiveness, and real-time capability, making it indispensable across a wide range of medical applications. By incorporating advanced deep learning (DL) and artificial intelligence (AI) methodologies, this thesis research aims to enhance the diagnostic accuracy and efficiency of existing US imaging analyses focusing on discriminative DL models. It also seeks to unlock new applications particularly considering generative DL models, thereby broadening the spectrum of ultrasound's utility in medical diagnostics.

The development of robust DL models and data processing pipelines that address the inherent limitations of current techniques for B-mode ultrasound image analysis is a central focus. Three distinct clinical contexts that each present their specific challenges are confronted and novel solutions are proposed. In particular, B-mode ultrasound imaging and DL applications are affected by issues such as operator bias, limited data availability, and the generalizability and explainability of AI solutions to multi-organ segmentation and classification tasks.

The first challenge of operator bias is tackled through the development of a novel method for training DL models for the clinical task of measuring Common Carotid Intima-Media Thickness (cIMT). Measuring cIMT with manual annotations results in suboptimal risk stratificatification using this biomarker and training DL models directly on manual annotations transfer the operator bias to the models predictions. The proposed method improves the segmentation accuracy of the DL model, using a hybrid of manual and computerized annotations to guide network's training. Moreover, a custom, task specific modification to Dice loss is proposed. These methods improve the segmentation performance of the DL model when tested in an external multi-center dataset achieving better correlation than manual operator when compared with the average of multiple readers.

The second issue of limited data availability is confronted through the development of a method for the automatic measurement of the Optic Nerve diameter (OND) and Optic Nerve sheath diameter (ONSD). To overcome the challenges brought by having a dataset with low numerosity and high variability, an innovative ensemble on UNet models was developed, validating the increase in segmentation performance with ONS and ONSD clinical endpoints.

The challenge of generalizability and explainability of DL solutions to multi-organ segmentation and classification tasks is addressed through the proposal of an end-to-end pipeline for the classification, segmentation, and characterization of muscle US images. This chapter expands current literature enabling the automatic classification and segmentation of up to 16 muscle groups while previous works typically focus only on a few muscle groups. A first of its kind radiomics-based approach using texture analysis of the segmented muscle and a machine learning model was developed to reproduce the Heckmatt score, a visual assessment scale of muscle condition. Explainability of the AI method was incorporated evaluating feature importance. The developed pipeline is hence able to provide an explainable and reproducible way for muscle analysis that improves manual scoring by quantitatively explaining a categorical grade.

Challenges encountered in earlier discussed applications, such as the variability in manual tracings of the Intima Media Complex segmentation, low signal-to-noise ratio in Optic Nerve Diameter (OND) measurements, and the complexity of segmenting multi-muscular B-mode images, underscore the limitations of discriminative models. These challenges arise from factors like underrepresentation in datasets, imprecise annotations, and suboptimal loss function selections, which collectively diminish model precision.

In order to take a step forward compared to discriminative models and address some of the limitations of these DL models in image analysis, generative models are explored. Generative models offer transformative solutions to these issues by enhancing image quality through denoising, standardization, and augmentation. Moreover, generative models provide the ability to create realistic medical images that can be used to validate discriminative models and develop simulator training tools for physicians. The final focus of this thesis is the development and proposal of a modular pipeline for medical image synthesis. This methodology proposes breaking down the image generation process into specific sub-tasks, enhancing both model training efficiency and control. Application of this pipeline to B-mode thyroid ultrasound imaging and digital pathology is proposed. The developed framework achieves realistic image generation correctly representing both healthy and pathological structures, and can be leveraged for decision support, as well as for training physicians and refining deep learning models.

In conclusion, this thesis captures the evolution of deep learning applications in medical B-mode ultrasound imaging, highlighting novel methodologies and the creation of a modular pipeline for image synthesis, aiming to improve diagnostics, physician training, and to extend the application of AI in enhancing patient care and medical education.