Project Title: **D**igital transformation in **A**rtificial-**I**ntelligence-based for **D**eformable registration in online **A**daptive **R**adiotherapy (D-AIDAR)

Supervisor: Pavel Dvořák

Co-supervisor: Petra Trnková

Brief introduction of the project

Radiotherapy planned on daily volumetric images offers superior plan quality tailored to each individual patient and current anatomical situation and potentially leads to reduced treatment side effects and probability of tumour recurrences[1,2]. However, it is very demanding on **fast and reliable digital workflows**. One of the most critical aspects is the accurate registration of different volumetric images that represent changes in anatomical situations between individual treatment fractions, enabling the correct accumulation of dosage throughout the overall treatment[3]. **Precise accumulation of dose is crucial for reliable evaluation of the dose delivered** to the healthy tissue surrounding the tumour, which leads to predicting treatment outcome and evaluating potential side effects[4].

Current image registration methods are either based on simple rigid shifts which are not suitable for variable anatomy between images, or image deformation using several different algorithms. **Deformable image registration (DIR)** methods are iterative optimization procedures that extract appropriate features, select a similarity measure for the evaluation of registration quality, and decide the transformation model[5]. However, existing DIR methods vary in accuracy, depend on operator expertise, and lack standardized validation in complex anatomical scenarios[6]. These limitations raise concerns about their reliability in dose accumulation and clinical applicability [7].

To address these challenges, we propose an **artificial intelligence (AI) driven DIR approach using Generative Adversarial Networks**[8,9]. This method enhances registration accuracy by generating anatomically precise displacement fields while reducing inter-operator variability. By integrating generative AI based DIR into online adaptive radiotherapy, we aim to improve dose conformity and facilitate multi-institutional standardization of treatment evaluation.

The unique collaboration between Czech Technical University in Prague (Prague, Czech Republic) (**CTU**) and Dong-A University (Busan, South Korea) (**DAU**) offers excellent opportunity to combine expertise in computational mathematics and clinical radiotherapy experience. **This partnership aims to address the comprehensive problematics of DIR and dose accumulation from different perspectives including real world clinical application with the development of cutting-edge digital technologies**.

Objectives

The aim of the proposed project is to develop and validate a method for DIR based on generative AI to increase the accuracy of dose accumulation in radiotherapy. The developed image registration must be reliable, operator and date set independent with robustly defined uncertainty and easy implementation at any institute. To achieve the aim, two main objectives will address the knowledge gaps connected to bringing DIR-based dose accumulation in online adaptive radiotherapy into clinical reality. Each objective will be addressed in work packages (section 3.1) comprising the systematic investigation of these aspects and can be summarized as follows:

- ***Objective 1: Novel generalizable DIR method based on generative AI:***

The aim is to develop a generative AI-based DIR method that can be generalized across different patient anatomies and imaging conditions. This method will use GANs to generate accurate deformation fields, ensuring reliable image alignment even in the presence of complex anatomical changes. It will focus on data efficiency, robust uncertainty quantification, and easy clinical implementation across various institutions.

- ***Objective 2: Accurate dose accumulation for online adaptive radiotherapy:***

The goal is to evaluate the accuracy of the novel DIR methods for a potential clinical application in dose accumulation during online adaptive radiotherapy. We will evaluate the uncertainties of the algorithm in comparison to existing methods. We will perform its validation on an independent patient data set.

The work program is organized in two main work packages (WPs), reflecting the project objectives introduced above and one management WP. In each WP, milestones have been formulated defining principal results. An overview of the project workflow can be found in Gannt chart.

WP3: Benchmarking of dose accumulation based on DIR using GAN (CTU)

This work package aims to benchmark the performance of DIR based on GANs developed in the WP2. The benchmark will be performed against commercially available systems and the suitability of GAN based DIR for (online) adaptive radiotherapy will be established.

Task:

- **Task 3.1: Digital phantom development:** The preliminary evaluation will be performed on a digital phantom mimicking the patient anatomy including the tissue composition with simplified organ shapes and clearly defined deformations to identify the source of uncertainty in the validation. Suitable phantom shape, composition and complexity will be defined within this step.

- **Task 3.2: Data Acquisition:** For the benchmark, real-world patient data treated for tumours in abdomen and pelvic region undergoing adaptive protocol will be collected. For each patient included in the study, all treatment planning CTs, including clinical contours and treatment plans will be anonymized and visually control to ascertain the suitability and completeness for the evaluation. No image processing (i.e. normalization, noise reduction, and data augmentation) will be performed to maintain the real-world quality of the data.
- **Task 3.3: Deformation and dose accumulation with commercially available software:** For both phantom and patient data sets DIR and dose accumulation will be performed with commercially available solutions: RayStation (RaySearch Laboratories, Sweden), ART-Plan (Therapanacea, France), MiM (MiM Software, USA), Eclipse (Varian, USA). The deformation vector field will be afterwards applied on the structure set as well as dose distribution and the difference among the commercial systems will be quantified using standard metrics for contouring accuracy evaluation and dose-volume parameters[28]. The results will be used for identification of the most robust method for evaluation and benchmarking.
- **Task 3.4: Evaluation of structure mapping:** Once the new algorithm is available, an initial evaluation of its performance will be done with the digital phantom. The phantom will be used for generation of several different datasets with various organ positions and shapes. Each organ will be segmented in every data. One dataset will be used as the reference one. The DIR will be applied to register all other datasets onto the reference one. The resulting deformation matrix will be used for mapping of all the segmented structures onto reference dataset. The quality of the mapped structures will be compared to the segmented structures on the reference dataset using the standard quality evaluation matrix[29]. The outcome will be feedbacked to the DIR developer in WP2 to address potential limitations of the DIR.
- **Task 3.5: Benchmarking against clinically systems:** The final evaluation will be performed on the patient data. For each patient, the original planning CT will be reference data sets. The deformation will be applied between the reference image dataset and all subsequent images. Resulting vector field will be used for structure mapping at first. The results will be compared to results from the commercial software using the standard matrics[29]. Afterwards, the vector field will be used for dose deformation. The outcome will be compared to commercial solutions using DVH metrics[28]. At the end a recommendation of the clinical applicability of hybrid GAN based deformation including its uncertainties and limitations will be derived. noise reduction, and data augmentation to improve the model's generalizability across diverse patient populations.

<u>Milestones:</u> **M3.1** – Digital phantom finalized; **M3.2** – High quality data set for development, validation and benchmarking available; **M3.3** – Developed method for validation; **M3.4** – Recommendations on applicability of the new DIR