Abstract

For high-precision radiation therapy (RT), it is critical to obtain an accurate and robust virtual representation of the patient, or patient model, as the foundation for clinical tasks. These models are typically constructed from volumetric medical images, primarily computed tomography (CT) and complemented by adjunct datasets such as magnetic resonance imaging (MRI) and positron emission tomography (PET) in the conventional RT workflow. This dissertation integrates several advanced imaging and novel computational techniques to construct robust patient models in support of key stages in a high-precision RT workflow under evolving treatment paradigms and imaging platforms.

To develop patient models for functional response assessment, a novel deep-learning-enhanced multi-parametric MR sequence (DL-MUPA) that yielded T1 and T2 relaxometry maps was evaluated. One-year phantom benchmarking demonstrated excellent longitudinal repeatability with inter-session coefficient of variation <7%. Evaluation in cohorts including patients with brain metastases and head and neck cancer (HNC) suggested high repeatability in uninvolved tissues and demonstrable changes in lesion (ΔT1/ΔT2 up to 40% at both sites) and organs adjacent to targets receiving radiation dose (ΔT1/ΔT2 up to 40%), highlighting the sensitivity of the functional MRI sequence and potential to identify actionable endpoints for functional treatment adaptation, pending validation in larger cohorts with clinical outcome data.

To develop robust patient models for accurate dose calculation for MRI-based applications, image synthesis tasks such as generating synthetic CTs are required for MR-guided radiation therapy (MRgRT). A conditional generative adversarial network (cGAN) was implemented to translate low-field MRI to CT to facilitate dose calculation in low-field brain MRgRT. The cGAN generated high-quality synthetic CTs (MAE=71 HU within the external relative to reference CTs) with strong dosimetric agreement (gamma pass rate >92% at 1%/1mm). External validation yielded no significant differences (P-value >0.05) with comparable dosimetric results, suggesting

great promise of implementing synthetic CTs to facilitate accurate dose calculation for online adaptive brain MRgRT.

For precise proton dose calculation, stopping power ratio (SPR) maps are required. We developed novel modality-agnostic deterministic regularized Brownian Bridge (rBBrg) diffusion model framework to directly predict SPR maps from routinely acquired cone beam CT (CBCT) or MRI datasets. Compared with conventional approaches that synthesize CT from a single input modality, our design bypasses CT number to SPR calibration, simplifying the SPR estimation workflow and reducing dependence on scanner- and protocol-specific HU calibration, and provides greater flexibility to support diverse clinical workflows. The rBBrg model was validated in a HNC patient cohort with model performance evaluated by mapping the predicted SPR back to HU numbers using an established calibration. The rBBrg model outperformed conventional Residual Network in CBCT-based SPR synthesis (MAE=52 HU within the external, improvement in MAE ~6%, P-value <0.05) while MRI-based SPR synthesis performance was comparable (MAE=84 HU, P-value >0.05). Dosimetric evaluation on a representative patient treatment plan (pre- and mid-treatment) showed strong agreement with gamma pass rate ~99% at 2%/2mm, demonstrating promise of rBBrg to support precise proton dose calculation for rapid adaptive proton therapy.

Another recent advancement in RT is the emergence of upright proton therapy (PT) enabled by novel upright positioning systems. To ensure safe implementation of upright PT, the reliability of physical property modeling on the novel upright CT requires comprehensive characterization for precise dose calculations. Longitudinal CT number stability was assessed over 8 months of operation which demonstrated minimal variations with inter-session CT number standard deviation <5 HU. CT number to SPR conversion was rigorously specified following established consensus guidelines. In-phantom proton dose calculation comparison showed excellent dosimetric agreement with conventional recumbent CT, with gamma pass rate >99% at 1%/1mm.

A major unmet need to enable upright PT is the limited availability of adjunct RT images including diagnostic CT, MRI and PET-CT in upright posture. A 3D cGAN-based lightweight model, UprightVision, was developed to predict a 3D displacement vector field (DVF) from the input supine dataset, which was used to warp the supine dataset to upright geometry. Evaluation in matched-pair supine-upright pelvic MRI datasets and thoracic CT datasets demonstrated the feasibility to predict the substantial anatomical changes with Dice similarity coefficient >0.7 between the predicted and ground truth key structures. The predicted DVF demonstrated smooth deformation with limited folding as indicated by percentage of voxels with negative Jacobian determinant <1% within the body external, which also enabled contour propagation and translation of co-registered supine datasets to facilitate downstream treatment planning workflows.

When taken together, this work demonstrates novel means of developing robust patient models that integrate physical, anatomical and physiological information to advance high-precision RT.