PhD Thesis Title: Development and Clinical Validation of Knowledge-Based Planning Models for Stereotactic Body Radiotherapy of Early-Stage Non-Small-Cell Lung Cancer Patients

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ABSTRACT:

Lung stereotactic body radiotherapy (SBRT) is a viable alternative to surgical intervention for the treatment of early-stage non-small-cell lung cancer (NSCLC) patients. This therapy achieves strong local control rates by delivering ultra-high, conformal radioablative doses in typically one to five fractions. Historically, lung SBRT plans were manually generated using 3D conformal radiation therapy, dynamic conformal arcs (DCA), intensity-modulated radiation therapy, and more recently via volumetric modulated arc therapy (VMAT) on a C-arm linear accelerator (linac). Manually planned VMAT is an advanced technique to deliver high-quality lung SBRT due to its dosimetric capabilities and utilization of flattening-filter free beams to improve patient compliance. However, there are limitations in manual treatment planning as the final plan quality heavily depends on a planner's skill and available planning time. This could subject the plan quality to inter-planner variability from a single institution with multiple planners. Generally, the standard lung SBRT patient "simulation-to-treatment" time is seven working days. This delays clinic workflow and degrades the quality of treatment by eliminating adaptive re-planning capabilities. There is an ongoing effort to automate treatment planning by creating a model library of previously treated, high-quality plans and using it to prospectively generate new plans termed model-based knowledge-based planning (KBP). KBP aims to mitigate the previously mentioned limitations of manual planning and improve the clinical workflow. As part of this dissertation, the lung SBRT KBP models were created using a commercially available KBP engine that was trained using the non-coplanar VMAT lung SBRT plans with the final dose reported from an advanced Acuros-based algorithm. The dissertation begins with the development of a robust and adaptable lung SBRT KBP model for early-stage, centrally-located NSCLC tumors that is fully compliant with Radiation Therapy Oncology Group (RTOG)-0813 protocol's requirements. This new model provided a similar or better plan quality to the clinical plans; however, it significantly increased the total monitor units and the plan's complexity. This prompted the development and validation of an automated KBP routine for SBRT of peripheral lung tumors via DCA-based VMAT per RTOG-0618 criteria. This planning routine helped to incorporate a historical DCA-based treatment planning approach with a VMAT optimization automated KBP engine that helps to reduce the plan's complexity. For both central and peripheral lung lesions, the validated models can generate high-quality, standardized plans in under 30 min with minimal planner effort compared to an estimated 129 ± 34 min of a dedicated SBRT planner's time. In practice, planners are expected to meticulously work on multiple plans at once, significantly increasing the manual planning time. Thus, these KBP models will shorten the "simulation-to-treatment" time down to as few as three working days, reduce inter-planner variability and improve patient safety. This will help standardize clinics and enable offline adaptive re-planning of lung SBRT treatment to account for physiological changes that cause errors resulting from improper patient set-up. Lastly, this dissertation sought to further expand these KBP models to support delivering lung SBRT treatments on a new O-ring linac that was recently introduced to support underserved areas and fast patient throughput. Despite learning from a C-arm modality training dataset, these KBP models helped the O-ring linac to become a viable treatment modality for lung SBRT by providing an excellent plan quality similar to a C-arm linac in under 30 min. These KBP models will

facilitate the easy transfer of patients across these diverse modalities and will provide a solution to unintended treatment course disruption due to lengthy machine downtimes. Moreover, they will relieve the burden on a single machine in high-volume lung SBRT clinics. Further adaptation and validation of these KBP models for large lung tumors (> 5 cm) with multi-level dosing scheme and synchronous multi-lesion lung SBRT is ongoing.

References to author publications that relate specifically to the thesis:

1. **Justin Visak**, Ronald C McGarry, and Damodar Pokhrel, "Clinical Evaluation of Photon Optimizer (PO) MLC Algorithm for Stereotactic, Single-Dose of VMAT Lung SBRT." Medical Dosimetry, 2020; 45(4): 321–326. https://doi.org/10.1016/j.meddos.2020.03.004

2. Damodar Pokhrel, **Justin Visak**, and Lana Sanford, "A novel and clinically useful dynamic conformal arc (DCA)-based VMAT planning for lung SBRT." J Appl Clin Med Phys, 2020; 21(7): 29–38. https://doi.org/10.1002/acm2.12878

3. **Justin Visak**, Ronald C McGarry, Marcus E Randall, and Damodar Pokhrel, "Development and Clinical Validation of a Robust Knowledge-Based Planning Model for Stereotactic Body Radiotherapy Treatment of Centrally Located Lung Tumors." J Appl Clin Med Phys, 2021; 22(1): 146-155. https://doi.org/10.1002/acm2.13120

4. Damodar Pokhrel, **Justin Visak**, Lana C Critchfield, Joseph Stephen, Mark E Bernard, Marcus Randall, and Mahesh Kudrimoti, "Clinical Validation of Ring-Mounted Halcyon Linac for Lung SBRT: Comparison to SBRT-Dedicated C-Arm Linac Treatments." J Appl Clin Med Phys, 2020; 22(1): 261-270. https://doi.org/10.1002/acm2.13146

5. **Justin Visak**, Gary Y Ge, Ronald C McGarry, Marcus Randall, and Damodar Pokhrel, "An Automated Knowledge-Based Planning Routine for Stereotactic Body Radiotherapy of Peripheral Lung Tumors via DCA-Based Volumetric Modulated Arc Therapy." J Appl Clin Med Phys, 2020; 22(1): 109-116. https://doi.org/10.1002/acm2.13114