Advancing Treatment Planning for Ultra-High Dose Stereotactic Ablative Radiosurgery (SABR)

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Objectives: This work functions as a follow-up treatment planning study improving previously developed approaches to treat patients with Immunotherapy in Combination with Ablative Radiosurgery to Ultra-high doSes (ICARUS). The original ICARUS planning study proved that a VMAT planning approach, coupled with a modern linear accelerator, could escalate radiation doses to more than 360Gy BED10 while maintaining normal tissue tolerances for tumors located in the abdomen, thorax, and pelvis. Prescribed dose for all plans on this study was 90Gy in 3 fractions, with plans designed for treatment via a LINAC.

This follow-up to the initial ICARUS study involves a multi-faceted approach. First, a second institution was tasked with replanning the original 15 patients on study. In accordance with an upcoming multi-institutional, phase 1 dose-escalation clinical trial to deliver ICARUS, normal tissue tolerances were updated to expand organs-at-risk (OARs) to planning OARs (PRVs) that could be affected by inter- and intra-fraction motion and changes in filling or were considered critical serial organs. The delivery of ultra-high dose while maintaining OAR dose tolerance to expanded OARs could impact the ability to deliver the prescribed dose to the subGTV targets used in the original study; subGTVs are spatially optimal contractions of gross tumor volumes that can aid in OAR sparing.

To combat the increased difficulty in delivering ultra-high dose SABR with expanded PRVs, a recent advancement in optimization was investigated to determine possible impact on planning cases per the ICARUS protocol. All plans on the follow-up study were optimized with the stereotactic normal tissue optimizer (SBRT NTO) in Eclipse v18.0.0 (Varian Medical Systems), which aims to reduce high dose spillage within the first 3mm outside of the target and low and intermediate dose spillage up to 2cm from the target. For ultra-high dose SABR, the potential to reduce high, intermediate, and low dose spillage is a major priority, and SBRT NTO could provide a pathway to improving dose falloff achieved in the original study.

Methods: The same 15 test cases from the original ICARUS study were used for planning. No changes to target volumes (subGTVs) from the original ICARUS study were made in the clinical plans. The subGTVs were originally contracted from gross tumor volumes more than 65cc; contractions were mostly isotropic, geometrically based reductions to ensure a target of roughly 5cm equivalent diameter. 5mm PRVs were added to the following OARs: stomach, duodenum, small bowel, and large

bowel. 3mm PRVs were added to the spinal cord, cauda equina, brachial plexus, and sacral plexus. The original dosimetric constraints for these OARs were applied to these PRVs.

Treatment planning was performed at the secondary institution utilizing an in-house Knowledge Based Planning (KBP) model adapted for ultra-high dose SABR. While the original study utilized 6-8 coplanar arcs, the updated ICARUS plans utilized 6-8 arcs in both coplanar and non-coplanar arrangements; virtual collision detection was utilized to ensure proper gantry-couch alignment. All plans utilized 6X-FFF or 10X-FFF arcs, depending on target depth. Plans were generated to deliver 90Gy in 3 fractions, with the goal of achieving ideal coverage of V100% ≥ 95% or an acceptable coverage of V70% ≥ 99%, per protocol.

All plans were generated for a Varian TrueBeam LINAC equipped with Millennium MLCs. Optimization and dose calculations were performed using Eclipse PO v18.0.0 and Acuros AXB v18.0.0., respectively. SBRT NTO was enabled in the optimization window, with a weighting of 150 for each case. In addition to SBRT NTO, monitor unit limits and aperture shape controller were utilized ("High" setting) to reduce MUs and plan complexity in an effort to reduce the interplay effects for moving targets and excessive leakage from high MU intrinsic to such high dose deliveries. Patient-specific quality assurance (PSQA) of the generated plans was performed using the ArcCHECK (Sun Nuclear Corporation) 3D diode array.

Results: Normal tissue tolerances were achieved for all 15 patients in the follow-up planning study. The prescribed subGTV coverage was achieved in 10/15 cases; the remaining five cases met or surpassed the variation acceptable coverage criterion. The subGTV coverage was limited in these five cases to ensure OAR tolerance, with skin affecting shallow targets in three cases (patients 1, 12, and 14) and bowel PRVs restricting subGTV coverage in three abdominopelvic cases (patients 2, 10, 14); skin was a dose-limiting OAR in patients 1 and 12 on the original study as well, whereas there was an absence of dose coverage limiting PRVs in that study.

Updated planning techniques and improvements in optimization and dose calculation algorithms had a positive impact on dose falloff, conformity, and efficiency. For the 10 cases where ideal coverage was achieved in both the original and current study, intermediate dose spillage was reduced, with gradient index improved by 0.68 on average (3.16±0.17 vs 3.83±0.48), D2cm reduced by 11% on average (55±3% vs 66±6.6%), and R50 reduced by 1.05 on average (4.10±0.67 to 3.05±0.17), for original vs. current study, respectively. The V105%, or high dose spillage outside of the subGTV, was reduced to less than 0.001, on average (goal of less than 0.15). Treatment delivery efficiency was improved with the introduction of non-coplanar beams, MU limitation, and aperture shape control; the updated plans show a reduction in modulation factor, from 3.08±0.76 (original) to 2.79±0.42 (current), on average, which corresponds to an average MU reduction of 900MUs. Both planning studies achieved similar max BED10, with the original achieving 552.3±114.4Gy, compared to 588.1±44.3Gy achieved in this study.

PSQA measurements with ArcCHECK yielded acceptable results, with clinical gamma pass rates of 99.1±1.3%, 98.1±1.5%, and 96.9±1.9% on average for 3%/2mm, 2%/2mm, and 3%/1mm gamma analysis criteria, respectively.

Conclusion(s): An ultra-high dose scheme of 90Gy in three fractions was proven dosimetrically feasible with a follow up planning study at a second institution using a newly released SBRT NTO and updated planning techniques. While skin and PRV structures limited subGTV coverage in 33% of the dataset, the planning techniques employed significantly improved dose falloff outside of the subGTV, which is extremely critical for patients receiving ultra-high dose SABR where the lower isodose lines now correspond to clinically appreciable doses. Any improvements providing sharper dose falloff

should have an impact on OAR and generic normal tissue dose reduction. Advancements in optimization algorithms and planning techniques have improved plan quality metrics across the patient cohort. Our team gained an understanding of the limitations of delivering ultra-high doses in this planning study, as the degree of difficulty in delivering ideal dose coverage was increased with the adoption of clinical OAR dose tolerances for expanded PRV structures for enhanced patient safety. As we prepare for the opening of a multi-institutional dose-escalation trial applying ultra-high dose SABR, it was important for other member institutions to feasibly plan these cases and demonstrate the potential for more widespread adoption. With the use of a KBP model, the updated plans were greatly standardized and exhibited less statistical variance; plans guided by KBP took 1-2 iterations to generate a successful plan. This could increase planning efficiency and serve as an education tool for colleagues participating in an upcoming multi-institutional clinical trial to deliver ultra-high dose SABR, while also providing an additional layer of uniformity and safety for patients on trial. With the planning improvements seen in this study, it is possible for other institutions to employ our KBP model and optimization techniques to safely plan and deliver ICARUS treatments.