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# The Role of Novel MLC-Based 3D-Conformal Spatially Fractionated Radiation Therapy (SFRT) Treatment in the Management of Large and Bulky Tumors

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**Abstract**
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## Abstract

Objectives:

Historically, our institution was a pioneer cancer center for treating large and bulky tumors (> 8 cm) for both palliative and therapeutic intents utilizing a spatially fractionated radiation therapy (SFRT) method called GRID therapy, which used a single-field Cerrobend GRID block and managed skin toxicity. In addition to direct cell-kill, SFRT promoted indirect cell-death via radiation-induced bystander signaling to adjacent tumor cells, upregulating various immunostimulatory cytokines and damaging intratumor micro-vasculature which contributed to dramatic regression of large tumor masses observed in the clinic. However, for deep-seated bulky masses, there were many limitations of this traditional single-field approach: deep-seated bulky tumors may only receive a third or less of the prescribed dose of 15 Gy; difficulty in managing skin toxicity when escalating the tumor dose and challenge of sparing immediately adjacent critical organs; physical GRID-block was not readily available to any community centers; weight of the GRID-block (~25 pounds) posed a serious safety concern to radiation therapy staff and for cancer patients at many slanted gantry angles; and due to the lack of commissioning and validation data of the physical GRID-block in the treatment planning system (TPS) no dosimetric details were readily available in the user's TPS for documentation of total monitor units and dose to critical organs for physician's plan review before SFRT delivery. Recently, inversely-optimized IMRT/VMAT, and Helical Tomotherapy SFRT plans or more advanced robotic CyberKnife unit, microbeam, or proton GRID therapy can be offered to the select SFRT patients. However, these modern SFRT methods may not be accessible for the same-day/next-day treatment due to their extensively long clinic work flow time for generating tumor lattice target structure and delineating critical organs, inverse-treatment planning and extensive patient-specific physics quality-assurance (QA) times. Moreover, every candidate SFRT patient may not have access to limited and expensive treatments such as CyberKnife or proton GRID therapy. To overcome these difficulties and address the immediate need for same-day/next-day treatment of SFRT to large and bulky tumors including deep-seated masses, we have developed and clinically implemented a novel MLC-based 3D-conformal planning and treatment delivery technique for our SFRT patients. Herein, we present the effect of adding a new MLC-based SFRT program to our institution and briefly analyze the patient reported clinical outcomes of our SFRT method.

Methods:

Utilizing an in-house MLC fitting algorithm, Millenium-120 leaves were fitted to the gross tumor volume (GTV) generating 1 cm diameter holes with 2 cm center-to-center spacing at isocenter. This technique utilizes up to 6 coplanar crossfire gantry angles 60o apart with a 90o collimator and differentially weighted 6 or 10 MV beams. This geometry allows corresponding matching MLC(s) on each opposing gantry-pair to open and block the required GRID contour without generating a lattice structure. A single-dose of 15 Gy was prescribed and calculated using advanced Acuros-based dose engine, generating sieve-like highly heterogenous dose tunnels within an hour of CT simulation permitting for same day SFRT treatment. Supplementing in-house testing and validation, to standardize and credential this method independently, we have irradiated site-specific (brain, head and neck, liver, lung, and pelvis) SRS/SBRT phantoms from the IROC MD Anderson's Houston QA center and received results that were acceptable for patient SFRT treatment. In the past 3 years, using this method we have treated more than 100 patients, comprising of multiple treatment sites (head and neck cancers, neglected breast masses, chest/lung tumors, abdominal/pelvis masses, liver tumors, adrenal masses, para-spinal masses, large sarcomas and extremities) with GTV tumor sizes ranging from 6.0–15.0 cm in diameter. The dosimetric parameters these MLC-based SFRT plans evaluated for are: peak-to-valley dose ratio (PVDR = GTVD10% ÷ GTVD90%), mean GTV dose, GTV V7.5Gy, maximum dose to skin and immediately adjacent critical organs following the RTOG-0915 trial

(Arm 1) and AAPM TG-101 protocol requirements. These treatments were delivered on TrueBeam Linac via conebeam-CT guidance and patients were set up and verified with 6DOF PerfectPitch couch corrections. These patients received consolidated radiation therapy treatment after receiving SFRT, typically, starting 2 days after the SFRT treatment for 30 Gy in 10 fractions (for palliative cases) and site-specific full prescription doses for therapeutic intents while respecting the OAR dose tolerances. Moreover, patients underwent post-treatment CT imaging in 3-month intervals to evaluate for tumor size regression and post-radiation radiation response. Outcomes reported include decreases in tumor shrinkage, pain control, and treatment related radiation-induced toxicity.

Results:

In the past 3 years, we have treated more than 100 patients via MLC-based SFRT with large and bulky tumors of various histologies (non-lymphomatous) in various treatment sites, except brain. Mean GTV-SFRT volume was 670.8 ± 415.7 cc (range, 131.1–1490.0 cc). This novel MLC fitting algorithm provided excellent dose parameters with mean GTV(V7.5Gy) and mean GTV dose of 55.2% and 8.3 Gy respectively of 15 Gy prescription doses and well-respected dose to adjacent critical organs. Average peak-to-valley-dose-ratio was 3.5. Mean beam-on time was 3.34 minutes. Overall treatment time including patient setup similar to SRT/SBRT, pre-treatment conebeam CT imaging, and patient re-positioning to beam-off was within 15 minutes treatment slot and patient set up errors were within departmental protocol requirement. The MLC-based SFRT treatments provided enhanced target dose for bulky masses including deep-seated large masses and spared skin and adjacent critical organs. Forty-seven of 100 SFRT patients of various disease sites were available for clinical follow up study. Median follow-up interval from treatment delivery day was 3 months (range, 0–24 months). All patients tolerated the MLC-based SFRT treatment well. Thirty of 47 (63.8%) patients received post-treatment CT imaging at 3-month interval. Tumor shrinkage was observed in 23/30 (76.6%) patients who underwent post-therapy evaluation. Improved pain relief was reported in 26/33 (78.8%) patients. Twenty (42%) patients were confirmed as deceased. Ten (21.2%) patients passed away before the 3-month follow-up, and five (10.6%) patients passed away after the 3-month follow-up, three (6.3%) of whom exhibited grade 1 skin toxicity. Amongst the 35 patients evaluated in total for post-radiation toxicity; acute toxicity included skin erythema (grade 1, n = 5; grade 3, n = 1) and grade 1 odynophagia (n = 1), and chronic toxicity included grade 3 wound complication (n = 1) and grade 4 necrotizing fasciitis of the neck (n = 1). Otherwise, 26/35 (74.2%) of clinically evaluated patients reported no post-radiation toxicities, and no grade 5 toxicities were observed.

Conclusion(s):

Management of large and bulky unresectable tumors for both palliative and therapeutic cases via same-day MLC-based 3D-conformal method was fast, safe, and effective treatment option that provided rapid-response of decreased tumor burden including deep-seated tumors. That added tumor response maybe due to radiation-induced indirect cell-death (in addition to direct cell-kill providing improved pain control, and generally low morbidity rates. If not treated with SFRT, these bulky tumors may receive suboptimal daily dose that may not produce adequate tumor response as reported here. This simple yet clinically useful method provided effective palliation for a wide range of tumor sites and disease types, reducing tumor burden and improving patient comfort and compliance. Minimal physics support and QA resources were needed by eliminating the need for longer contouring and inverse-treatment planning and optimization, allowing for fast and effective clinical workflow allowing this SFRT method a “same-day” treatment. We suggest other institutions including community centers to commission and validate this MLC-based SFRT method at their C-arm Linac(s) for their patients. This could provide the highest-quality and most efficient SFRT treatment to underserved patient cohort with large and bulky unresectable masses together with neoadjuvant therapy including deep-seated tumors with no additional cost.