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Stereotactic Centralized Ablative Radiation Therapy - A Novel Methodology in Treating Bulky Tumor and Its Technical Realization

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Abstract
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Jun Yang [1] , Weisi Yan [2] , Qiuxia Lu [3] , Weihua Qi [3] , Fei Yu [4] , Yuan Li [3] , Sida Li [3] , Hongyin Cheng [3] , Jiayi Liu [5] , Xiaodong Wu [6]

1. Philadelphia Cyberknife, Philadelphia CyberKnife, Havertown, USA 2. Radiation Oncology, Baptist Health, Corbin, USA 3. Radiation Oncology, Foshan Chancheng Hospital, Foshan, CHN 4. Radiation Oncology, Quanzhou BinHai Hospital, Quanzhou, CHN 5. Nuclear Medicine, University of Pennsylvania, Philadelphia, USA 6. Radiation Oncology, Innovative Cancer Institute, Cyberknife Center of Miami, South Miami, USA

Corresponding author: Jun Yang, junbme@yahoo.com

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Abstract

Objective: SFRT (Spatially fractionated radiation therapy), such as GRID or LATTICE, is important in its concept of covering whole or partial tumor with inhomogeneous radiation dose to control the bulky tumor and, hopefully, trigger anti-tumor immuno-response. Even though the clinical benefits has demonstrated in the "bulky" tumor settings, the optimal dose and fractionation of SFRT is yet to be explored. A prospective, multi-center, dose-escalation trial was initiated, where we propose a new treatment methodology (called Stereotactic Centralized Ablative Radiation Therapy or SCART) for large tumor, which is based on the principles of SFRT, by using SBRT methods to deliver an ablative radiation dose to central portion of target (defined as sPTV) while keeping the dose to surrounding normal tissue to relatively low level.

Methods: Patients with unresectable solid bulky malignancies with limited treatment options were enrolled. Six dose-levels were proposed, with starting dose level 1 of 15 Gy to central spot sPTV in one fraction, level 2 of 15GyX2, level 3 of 15GyX3, level 4 of 18GyX3, Level 5 of 21GyX3 and Level 6 of 24GyX3. The peripheral dose at the tumor edge was limited at 5Gy each fraction.
A modern Linac with 5mm-leaf MLC was used to deliver the SCART treatment using VMAT technology. A spindle-shape sPTV was generated in the center of the GTV in the Treatment Planning System. The length of spindle is a few mm shorter than GTV in the SI direction to accommodate setup uncertainty. The diameter of the spindle sPTV is proportional to the dimension of GTV in axial view, and this proportion is determined by the ratio of tumor edge dose to the SCART prescription dose. Eclipse treatment planning system was used to generate VMAT plan with MLC's maximum opening size limited to the projection of sPTV, and 5Gy per fraction was defined as dose constraints to the surrounding tissue. 3D CBCT Image guidance was applied every treatment.

Results: Thirty-four intracranial and extracranial patients received SCART treatment in this study, with the mean volume of the target of 664 cc (Range, 11.6~ 3024 cc). The mean prescription dose was 15.9 Gy and 2.4 fractions. Average MU is 4500 per fraction, and average beam-on time is 7.5 min and the average treatment time is 18.5 min.
Radiotherapy was well tolerated with all treatment completed as scheduled. Patients who have long term follow up showed that 5/14 achieved PR, 3/14 achieved CR and 6/14 were SD, no PD was observed in patients treated.

Conclusion: VMAT technology is sufficient to generate the ultra-inhomogeneous SCART dose to a sPTV with fast dose fall-off to spare the surrounding tissue. SCART is feasible in both planning and delivery. It is effective with remarkably low toxicity rates and high local control rates. Multiple courses were applied to few patients and found safe. Maximum Tolerate Dose for SCART is yet to be established with ongoing trial.