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Practical Considerations for LATTICE Radiotherapy to Extremely Large Target Volumes

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Guozhen Luo [1], Somayeh Taghizadehghahremanloo [1], Ryan Brunkhorst [1], Adam D. Yock [2], Kenneth Homann [1], Eric Shinohara [1], Ryan Whitaker [3 3]

1. Radiation Oncology, Vanderbilt University Medical Center, Nashville, USA 2. Department of Radiation Oncology, Vanderbilt University Medical Center, Nashville, TN, USA 3. Radiation Oncology, Vanderbilt, Nashville, USA

Corresponding author: Guozhen Luo, guozhen.luo@vumc.org

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Abstract

Objectives:

Treating bulky tumors has long been challenging due to their large size and inherent proximity to critical organs. Recently, 3D LATTICE radiotherapy, a development from 2D GRID therapy, has garnered increased interest for its ability to treat these tumors with fewer side effects and improved local control.
Advances in modern technologies, including enhanced hardware (e.g. higher definition multi-leaf collimators (MLCs)) and improved software (e.g. better VMAT optimization algorithms) have made 3D LATTICE radiotherapy more accessible and easier to implement in most clinical settings. LATTICE radiotherapy has been demonstrated in small series to have improved response rates and local control compared to standard palliative radiotherapy. While the biology of these responses is under active investigation, preclinical evaluation hints at improvement activation of bystander effects and immune-mediated cell death. Thus, LATTICE in combination with immune checkpoint inhibitors and other immune-modulating agents could provide improved responses for patients with large and/or unresectable tumors. In this project, we report our institutional experience in treating extremely large target volumes with LATTICE radiotherapy and the practical considerations in treatment planning and quality assurance.

Methods:

LATTICE radiotherapy was implemented in our clinic in October 2023. Since then, a total of 10 patients have been treated for tumors in the chest, abdomen, or pelvis. The most common histology treated was soft tissue sarcoma (40%). VMAT delivered on the Varian TrueBeam platform, planned with Eclipse version 16, was utilized for all treatments. LATTICE radiotherapy was delivered with a dose of 20-30 Gy in a single fraction to vertices distributed throughout the target followed by a palliative regimen delivered to the entire GTV (median dose of 20 Gy in 5 fractions). All vertices were spheres with a diameter of 1.5 cm, manually placed as high-resolution structures according to three rules: all targets must be at least 1 cm away from any critical organs, a minimum center-to-center distance of 3 cm in 3D and a minimum center-to-center distance of 6 cm on the same axial plane. The GTV volumes ranged from 546 cc to 9,032 cc, and the number of vertices varied from 7 to 78. Following treatment planning, patient-specific QA was performed using portal dosimetry in accordance with our standard in-house protocol before treatment.

Results:

The ideal dose distribution for LATTICE aims to minimize the dose between the target areas while ensuring proper coverage to the targets. This approach maximizes the peak and valley effect, which may be implicated in potential bystander and immune effects of LATTICE RT. Our findings indicate that the complexity of treatment planning increases significantly when dealing with increased target size and number of vertices. For example, one patient presented with a very large unresectable soft tissue sarcoma of his pelvis and right lower extremity. The GTV volume of this tumor was 9,032 cc with 78 vertices placed for LATTICE boost. Due to the extremely large volume, several challenges emerged.
First, targets extended beyond the size that could be covered by a single isocenter. To address this, vertices were divided into two groups along the superior-inferior direction, with each group covered by separate isocenters. The two plans with 6 and 7 arcs, respectively, were then independently optimized independently. Given the relatively large distance between each target, the dose contribution from one isocenter to the other was negligible.
The second challenge presented when the large number of targets led to failure of GPU optimization due to insufficient memory. To overcome this, the optimization resolution was adjusted from 0.125 cm to 0.25 cm. This change reduced the memory requirement to one-eighth of the original, enabling the GPU optimization

to proceed and significantly reduced the optimization time. For the final calculation, we used the same AAA algorithm with a 0.125 cm resolution, in accordance with our standard, ensuring that the calculation accuracy was not compromised.
The third challenge was the number of monitor units (MU) required to cover all 78 vertices, which amounted to 54,158 MU. To minimize delivery time, we selected a 6FFF beam with the highest available dose rate of 1400 MU/minute.
Following successful quality assurance with portal dosimetry, the treatment plans were delivered in a single fraction. The time from the initial Cone Beam Computed Tomography (CBCT) scan to the completion of the final arc was 84 minutes. Patient was seen in follow-up with repeat imaging at 4 weeks which demonstrated partial imaging response with significant improvement of lower extremity edema and pain. Toxicity was manageable with expected G2 dermatitis and GI toxicity given tumor involvement of these OARs. Patient continues to demonstrate treatment response now approximately 4 months out from LATTICE RT.

Conclusion(s):

Our results demonstrate that LATTICE RT remains feasible even for extremely large GTVs and is associated with good clinical responses with manageable treatment related toxicity. In our series, better than anticipated imaging and clinical responses compared to standard palliative RT were observed with no G3+ adverse events. However, treatment planning and delivery for large LATTICE cases are significantly more complex and time-consuming. Extra care is essential to ensure a successful treatment plan and execution. Future work is needed to optimize the planning and delivery process to increase efficiency, including evaluation of implementation of higher energy FFF beams, automation/optimization of vertex structure, and examination of alternative LATTICE architectures. Finally, prospective evaluation of LATTICE radiotherapy alone or in combination with targeted systemic therapies is critically needed to determine the clinical value of these approaches.