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Concept to Clinic: Introducing Spatially Fractionated Radiation Therapy

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ABSTRACT

Purpose: To establish a practical framework for implementing spatially fractionated radiation therapy (SFRT) in clinics without existing infrastructure by developing treatment planning workflows and identifying requirements for clinical adoption.

Methods: A GRID therapy planning workflow was developed by importing commercial collimator beam data files into the research version of RayStation TPS and investigating planning parameters. Lattice radiotherapy was investigated using VMAT and IMRT techniques. Treatment plans were created and validated on an anthropomorphic Rando phantom with film dosimetry. Immobilization considerations and QA requirements for SFRT delivery were evaluated. Current clinical trial guidelines and recommendations from emerging SFRT task groups were reviewed to assess consensus and barriers to widespread adoption.

Results: GRID collimator beam data were successfully imported and modeled in RayStation, enabling treatment planning capabilities. Lattice VMAT and IMRT plans demonstrated the feasibility of achieving spatially modulated dose distributions. Film dosimetry on Rando phantom validated planned dose patterns. Analysis identified key QA requirements, including patient-specific verification and delivery validation protocols. A review of SFRT literature revealed an evolving consensus on prescription practices, but ongoing debate regarding optimal fractionation schedules and patient selection. Primary barriers to clinical adoption included limited equipment availability, training requirements, and lack of standardized commissioning and clinical implementation guidelines.

Conclusion: This work provides a foundation for centers considering SFRT implementation. The planning workflows and QA framework established here address practical implementation challenges. Future standardization efforts by active task groups will be essential for generating clinical evidence and enabling broader adoption of SFRT techniques.

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INTRODUCTION

Spatially Fractionated Radiation Therapy (SFRT) is a treatment technique that intentionally delivers a heterogeneous dose distribution consisting of high-dose peaks separated by lower-dose valleys. Unlike conventional radiotherapy, SFRT uses spatial dose modulation to deliver ablative doses while potentially improving normal tissue tolerance. Although the radiobiology remains under investigation, proposed mechanisms include vascular preservation, bystander effects, vascular disruption, and immune activation.

Modern implementations of SFRT include three techniques. Physical GRID uses a perforated high-density collimator to create a two-dimensional beamlet pattern but requires dedicated hardware and commissioning. MLC-based GRID recreates similar dose distributions using conventional multi-leaf collimators, eliminating dedicated hardware while enabling patient-specific beam shaping. Lattice radiotherapy extends spatial fractionation into three dimensions by placing high-dose spherical vertices throughout the gross tumor volume using VMAT or IMRT.

Despite increasing clinical interest, implementation remains limited by the lack of standardized commissioning procedures, treatment planning workflows, quality assurance recommendations, and efficient planning tools. This work investigates implementation strategies for physical GRID, MLC-based GRID, and lattice radiotherapy through the development of commissioning workflows and automated RaySt ation scripting tools.

METHODS AND MATERIALS

This study evaluated three SFRT implementation strategies in RayStation (RaySearch Laboratories, Stockholm, Sweden) using a commissioned Varian Edge beam model: GRID collimator commissioning, MLC-based GRID, and VMAT-based lattice radiotherapy.

No physical GRID collimator was available, so this portion focused on a proposed commissioning and QA framework and on approximating collimator geometry within the TPS using constructed 3D models.

MLC-based GRID used opposing AP/PA fields with rotated apertures at 0.5, 1, and 2 cm spacing, evaluated using peak-to-valley dose ratio (PVDR) and dose statistics, including a small-target test case to probe the technique's lower size limit.

Lattice plans placed spherical high-dose vertices within the GTV using custom RayStation scripts. These scripts automated sphere placement, progressing from uniform spacing to adaptive, tolerance-based placement, and a final version extended this into a basic VMAT auto planning workflow.

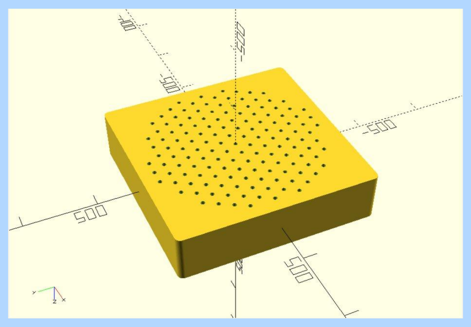

Figure 1. Simplified Grid Collimator Model

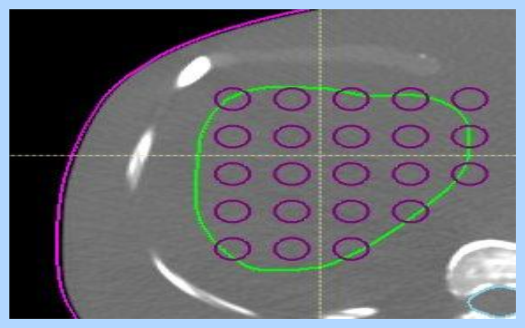

Figure 2. Example Unscreened ROIs

RESULTS

A commissioning and QA framework was developed for GRID collimators. Virtual collimator modeling was geometrically feasible but could not be integrated as a functional TPS structure.

For MLC-based GRID, PVDR rose from 1.53 to 5.86 as aperture spacing increased from 0.5 cm to 2 cm. This was driven mainly by falling valley dose, while peak dose stayed relatively stable, showing that spatial modulation is controlled primarily through geometry.

Dose grid resolution also mattered. At fixed 2 cm spacing, PVDR rose from 5.61 to 5.86 as the dose grid was refined from 0.3 cm to 0.2 cm, with little further change at 0.1 cm.

In a small target (about 2.7 cm), neither spacing produced a well-defined GRID pattern. At 1 cm spacing, too few apertures fit within the target. At 0.5 cm spacing, peaks and valleys merged toward uniformity.

Lattice sphere placement scripting progressed from uniform spacing to adaptive, tolerance-based placement, and a preliminary auto planning script automated structure generation, prescription setup, and basic VMAT optimization.

Table 1. PVDR Versus Spacing for Large and Small Target

	Large (1,2,4)	Small (1,3)
Spacing 1	1.53	1.44
Spacing 2	2.7	3.75
Spacing 3	5.86	N/A

Table 2. PVDR Versus Dose Grid

Dose Grid	PVDR
0.3 Dose Grid	5.61
0.2 Dose Grid	5.86
0.1 Dose Grid	5.85

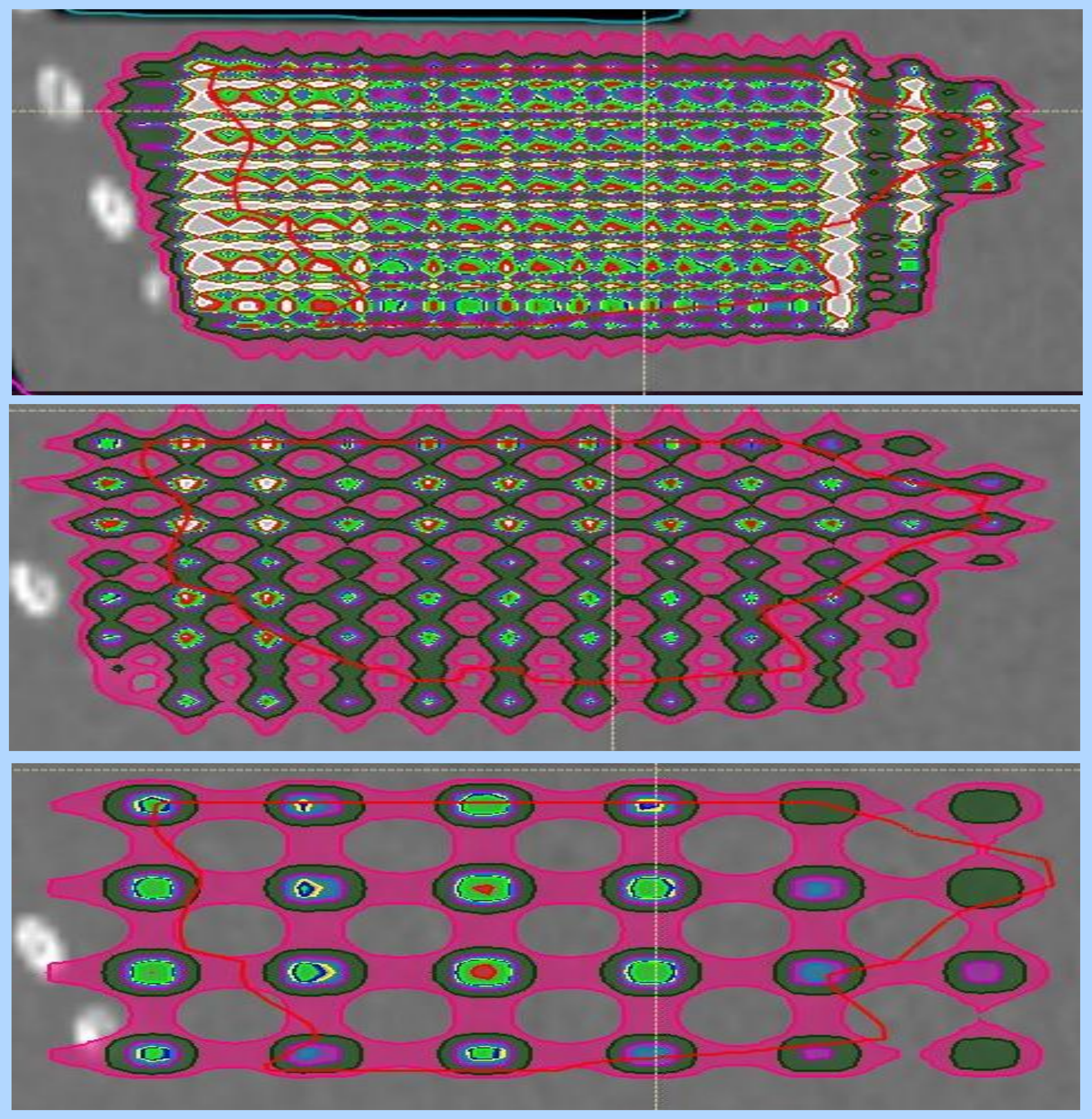

Figure 3-5. Alternating MLCs with increasing distance (1, 2, and 4 leaves)

DISCUSSION

For MLC-based GRID, larger aperture spacing produced stronger spatial fractionation, with the largest spacing tested coming closest to a clinically typical GRID pattern. This trend was driven mainly by decreasing valley dose, while peak dose stayed comparatively stable. Showing that PVDR in this technique is controlled primarily through geometry rather than beam weighting.

This trend did not hold in a much smaller target. Neither spacing option tested was well matched to that target: one left too few apertures within the target to form a repeating pattern, and the other was dense enough that peaks and valleys merged. This shows that the ratio of spacing to target size, not spacing alone, determines whether MLC-based GRID can generate a valid spatial dose pattern.

Lattice sphere placement scripting began by generating a large number of candidate sphere ROIs within the target, based only on diameter and side-to-side spacing. Successive script versions layered on constraints, including margins, axial and adaptive spacing, fractional containment within the target, and optional organ-at-risk avoidance, and target number of spheres as options to narrow that candidate pool down to a reasonable number of spheres. Not every rule determining how candidates should be rejected during this process was explicitly stated by the referenced research (so you have more ROIs than you should), so a summary of the process is created at the end of the script for reproducibly. A preliminary auto planning script extended this framework into basic structure and beam setup, but automation of the full optimization process was not fully completed and the resulting plans required manual refinement.

CONCLUSIONS

SFRT can be implemented using existing clinical tools, including MLC-based GRID and VMAT-based lattice techniques, without dedicated hardware. MLC-based GRID allows controllable spatial dose modulation through aperture spacing, but is limited by a minimum target size. Dose grid resolution meaningfully affects PVDR and should be held consistent across plan comparisons. Custom RayStation scripting can automate and standardize lattice sphere placement and provides a starting framework for VMAT auto planning. Together with the proposed GRID commissioning framework, these workflows provide a practical foundation for clinical SFRT adoption. Continued standardization, validation, and clinical studies are the next steps toward broader implementation.

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