

## ABSTRACT

**Purpose:** Spatially fractionated radiation therapy (SFRT) aims to deliver high-dose peaks within tumors while maintaining low-dose valleys. However, no consensus metric exists to define SFRT plan quality, and commonly used peak-to-valley ratios derived from gross tumor volume (GTV) DVHs fail to account for spatial dose heterogeneity and geometric constraints. We propose a structure-specific, multi-metric framework to guide SFRT planning and distinguish acceptable from suboptimal plans.

**Methods:** SFRT plans were retrospectively generated for 11 patients prescribed 15 Gy to the combined vertex volume (PTV\_ALL) and 3 Gy to the GTV, with 95% coverage using uniformly placed lattice vertices. Peak dose was characterized as D10 of PTV\_ALL. Valley regions were defined using two tumor substructures: GTV\_Control (GTV minus a 6-mm expansion of PTV\_ALL) and an intermediate-distance valley shell, 2CM\_Control (the region 6 mm–2 cm from PTV\_ALL within the GTV). A local peak-to-valley dose ratio (PVDR\_local) was defined as  $D10(PTV\_ALL)/D90(2CM\_Control)$ .

**Results:** Average vertex count, diameter, inter-vertex separation, and density were  $9.9 \pm 5.6$ ,  $1.6 \pm 0.4$  cm,  $2.4 \pm 0.9$  cm, and  $1.8 \pm 1.5$  vertices/100cc, respectively. PVDR\_local ranged 4.5–6.0 (mean  $5.3 \pm 0.6$ ). Mean dose to 2CM\_Control and GTV\_Control was  $5.70 \pm 0.94$  Gy and  $5.21 \pm 0.76$  Gy. The conventional GTV-based D10/D90 ratio was  $3.3 \pm 0.3$ . PVDR\_local showed a stronger, more interpretable relationship with 2CM\_Control dose than D10/D90; plans with PVDR\_local < 4.9 had the highest 2CM\_Control doses (>6.3 Gy), a pattern not captured by D10/D90.

**Conclusion:** Conventional PVDR metrics alone are insufficient to characterize SFRT plan quality. A structure-specific, multi-metric framework incorporating vertex coverage, PVDR<sub>local</sub>, and valley dose burden offers a practical, reproducible approach for guiding SFRT planning and evaluating plan quality.

## CONTACT

Salim Balik, PhD  
salim.balik@med.usc.edu

# A Framework for Assessing Plan Quality In Spatially Fractionated Radiation Therapy

Salim Balik, PhD, Hualin Zhang, PhD, Zhengzheng Xu, PhD, Zhilei Liu Shen, PhD, Kaley E. Woods, PhD, Benjamin P. Ziemer, PhD, Joshua Schiff, MD, Kenneth Wong, MD, Hirsch Matani, MD, Jason Ye, MD, Elizabeth Zhang-Velten, MD, May Tao, MD and Lauren Lukas, MD

Keck School of Medicine of USC, Los Angeles, CA

# INTRODUCTION

Spatially fractionated radiation therapy (SFRT) delivers focal high-dose peaks at lattice vertices while sparing intervening tumor tissue as low-dose valleys — spatial dose modulation thought to enhance immune-mediated and bystander tumor response.

Despite growing clinical use, no consensus metric defines SFRT plan quality. Conventional peak-to-valley dose ratios (D10/D90, D5/D95) are typically derived from whole-GTV DVH statistics, which conflate immediate-vertex peaks with distant, geometry-limited tumor regions that vertex placement was never intended to reach. This global averaging obscures the spatial dose modulation that SFRT planning actually controls, and can misrepresent plan quality when vertex geometry, spacing, or tumor shape varies across patients. We hypothesized that defining valley dose using anatomically meaningful, distance-based tumor subregions — rather than the whole GTV — would produce a peak-to-valley metric that more directly reflects planner-controllable dose fall-off, and would better distinguish clinically acceptable SFRT plans from suboptimal ones.

## METHODS AND MATERIALS

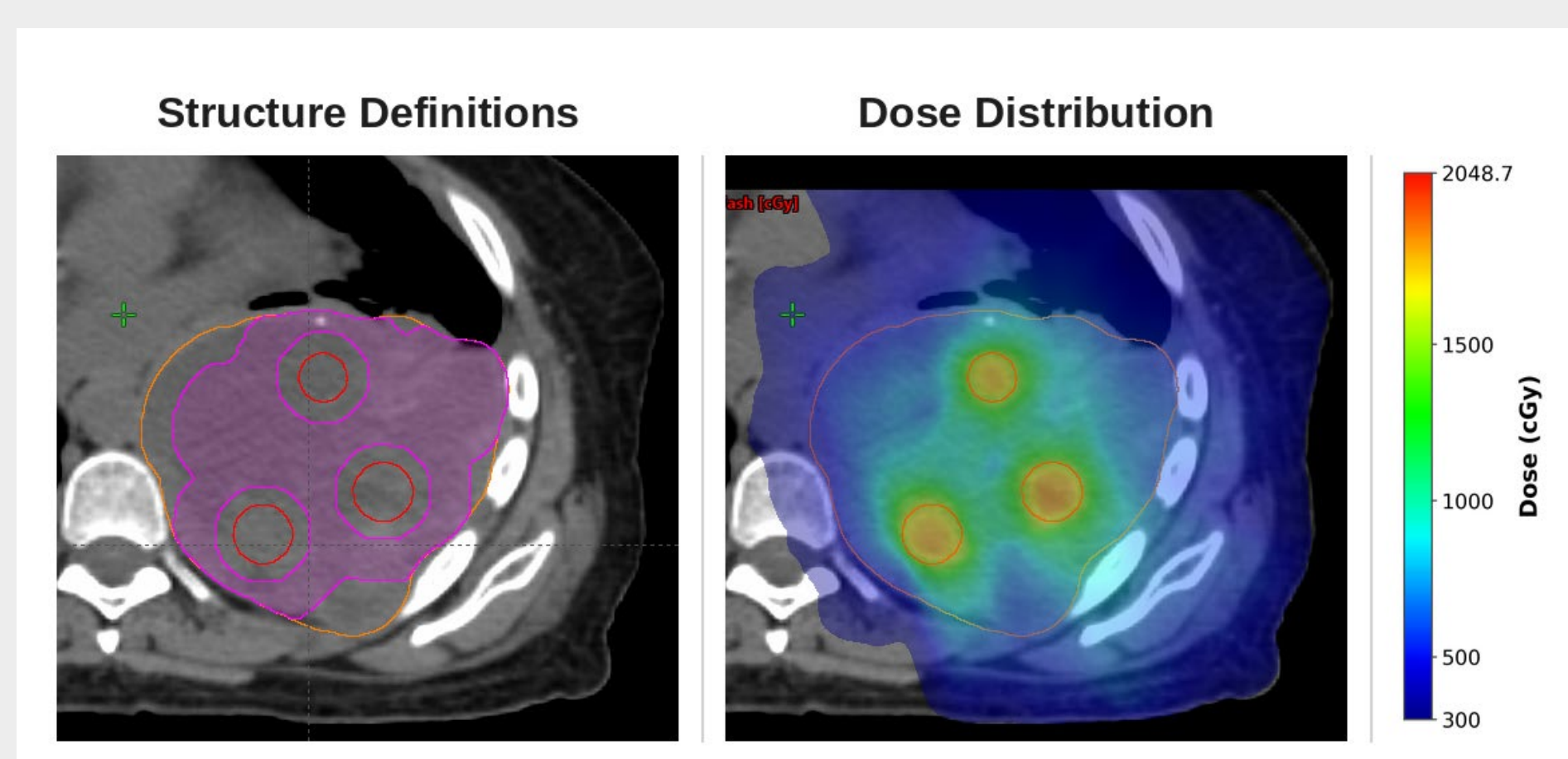
SFRT plans were retrospectively generated for 11 patients prescribed 15 Gy to the combined vertex volume (PTV\_ALL) and 3 Gy to the GTV, using a scripted algorithm to place lattice vertices uniformly throughout the GTV with 95% target coverage.

Two anatomically defined valley substructures were created for each plan:

- $GTV\_Control = GTV\_SFRT - (PTV\_ALL \text{ expanded } 6 \text{ mm})$ : tumor tissue outside immediate vertex influence.
- $2CM\_Control = [(PTV\_ALL \text{ expanded } 2 \text{ cm}) \cap GTV\_SFRT] - (PTV\_ALL \text{ expanded } 6 \text{ mm})$ : an intermediate-distance valley shell 6 mm–2 cm from the nearest vertex — the “reachable” fall-off region, excluding both immediate peaks and distant, geometry-limited tumor.

Peak dose was characterized as D10(PTV\_ALL). A local peak-to-valley dose ratio was defined as  $PVDR_{local} = D10(PTV\_ALL) / D90(2CM\_Control)$ . For comparison, the conventional D10/D90 ratio of the GTV was also calculated.

Vertex geometry (count, diameter, inter-vertex separation, and density per 100 cc of GTV) was recorded for each plan and related to PVDR\_local, D10/D90, and mean dose to 2CM\_Control and GTV\_Control.



**Figure 2.** Representative axial CT showing lattice vertices/PTV\_ALL (red), 2CM\_Control shell (magenta), and GTV\_SFRT (orange) (left); spatially co-registered dose colorwash (right) with dose scale (cGy).

## RESULTS

Across 11 patients, vertex count, diameter, inter-vertex separation, and density averaged  $9.9 \pm 5.6$ ,  $1.6 \pm 0.4$  cm,  $2.4 \pm 0.9$  cm, and  $1.8 \pm 1.5$  vertices/100cc (Table 1). PVDR\_local ranged 4.5–6.0 (mean  $5.3 \pm 0.6$ ), compared with a conventional GTV-based D10/D90 of  $3.3 \pm 0.3$ . Mean dose to 2CM\_Control and GTV\_Control was  $5.70 \pm 0.94$  Gy and  $5.21 \pm 0.76$  Gy.

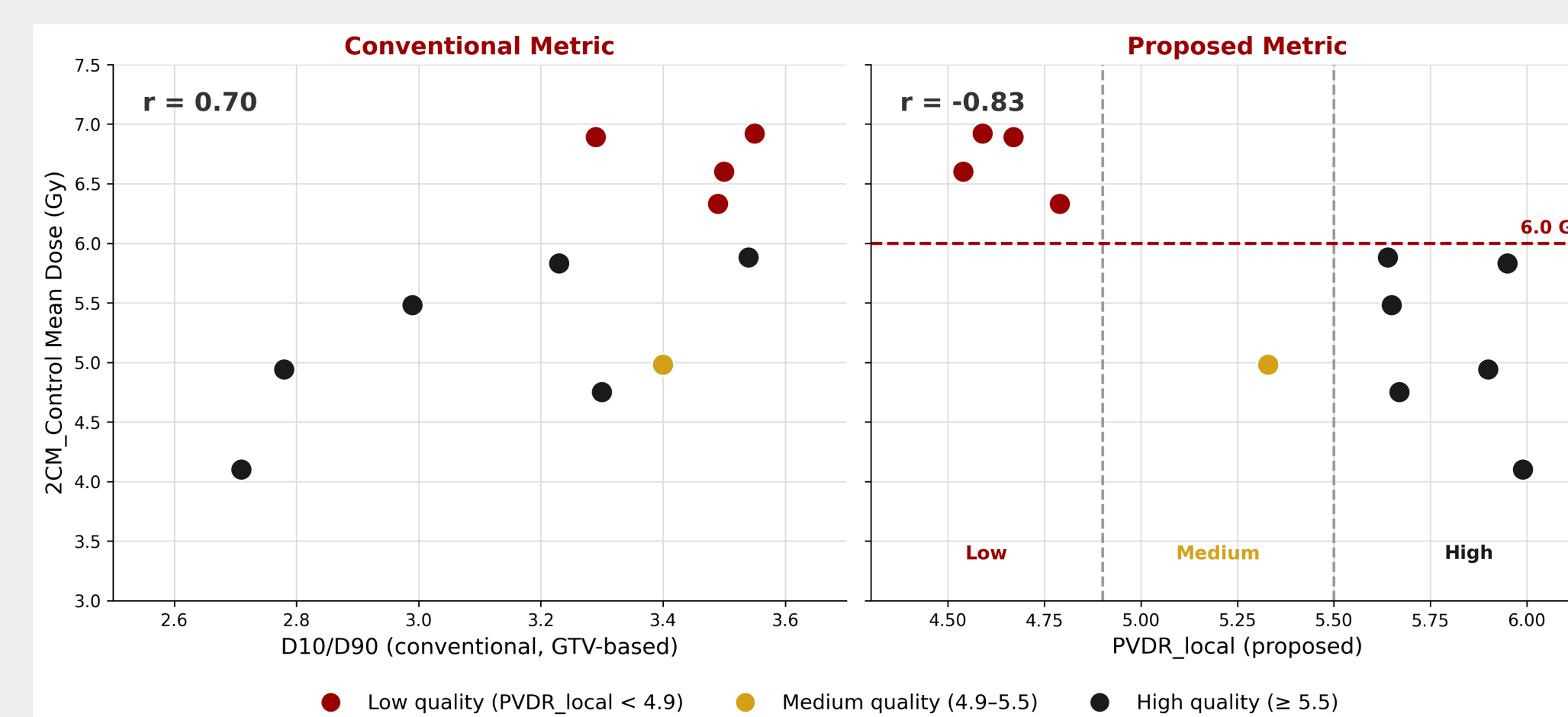
PVDR\_local demonstrated a stronger, more interpretable inverse relationship with 2CM\_Control dose than D10/D90 (Figure 1): higher PVDR\_local was consistently associated with lower 2CM\_Control dose, cleanly separating plans into low-, medium-, and higher-quality tiers.

Plans with PVDR\_local < 4.9 exhibited the highest 2CM\_Control doses (>6.3 Gy). No comparable separation was observed using D10/D90, which showed a weaker, noisier trend and failed to distinguish plans with similar vertex coverage but substantially different spatial dose distributions.

**Table 1.** Patient-specific SFRT parameters, sorted by PVDR\_local. Quality Tier follows the same thresholds as Figure 1.

| Patient | #Vert | Diam(cm) | Sep(cm) | D90(2cm) | D10/D90 | PVDR_loc | Tier |
|---------|-------|----------|---------|----------|---------|----------|------|
| 11      | 18    | 1.95     | 2.0     | 3.7      | 3.50    | 4.54     | Low  |
| 3       | 20    | 1.95     | 2.5     | 3.9      | 3.55    | 4.59     | Low  |
| 4       | 14    | 1.91     | 2.0     | 3.9      | 3.29    | 4.67     | Low  |
| 8       | 8     | 1.55     | 2.0     | 3.5      | 3.49    | 4.79     | Low  |
| 1       | 3     | 1.45     | 1.2     | 3.5      | 3.40    | 5.33     | Med  |
| 2       | 13    | 1.95     | 2.0     | 3.2      | 3.54    | 5.64     | High |
| 9       | 7     | 1.45     | 2.5     | 3.2      | 2.99    | 5.65     | High |
| 7       | 5     | 0.96     | 1.5     | 3.1      | 3.30    | 5.67     | High |
| 10      | 9     | 1.47     | 3.0     | 3.0      | 2.78    | 5.90     | High |
| 5       | 6     | 1.96     | 2.0     | 3.1      | 3.23    | 5.95     | High |
| 6       | 6     | 0.90     | 2.0     | 3.0      | 2.71    | 5.99     | High |
| Mean    | 9.9   | 1.59     | 2.06    | 3.43     | 3.25    | 5.34     | —    |
| SD      | 5.6   | 0.40     | 0.48    | 0.32     | 0.30    | 0.58     | —    |

#Vert = number of lattice vertices; Diam = vertex diameter; Sep = minimum inter-vertex separation; D90(2cm) = D90 dose to the 2CM\_Control shell (Gy); PVDR\_loc = D10(PTV\_ALL)/D90(2CM\_Control); D10/D90 = conventional GTV-based ratio; Tier = plan quality tier (Low <4.9, Medium 4.9–5.5, High ≥5.5).



**Figure 1.** Mean 2CM\_Control dose vs. D10/D90 ( $r = 0.70$ ) and PVDR\_local ( $r = -0.83$ ). Dashed lines mark quality tiers (PVDR\_local: 4.9, 5.5) and the 6.0 Gy valley-dose threshold; higher-quality plans cluster in the lower-right.

## DISCUSSION

This work introduces a structure-specific framework for evaluating SFRT plan quality. By defining valley dose using anatomically meaningful tumor subregions — rather than the whole GTV — and incorporating the geometric characteristics of lattice design, PVDR<sub>local</sub> links spatial dose modulation directly to a clinically relevant, intermediate-distance valley region.

Compared with traditional global heterogeneity metrics such as D10/D90, PVDR\_local showed a stronger and more interpretable relationship with mean dose to the 2CM\_Control shell, a region hypothesized to influence biological response to SFRT. This structure-specific approach enables objective discrimination between plans with similar prescription coverage to the vertices but substantially different spatial dose distributions — a distinction whole-GTV metrics cannot make.

Because peak dose in SFRT is inherently constrained by prescription and maximum-dose limits, PVDR alone cannot fully characterize plan quality: two plans with identical PVDR<sub>local</sub> may still differ in how much valley tissue is “flooded” with dose. We therefore favor a multi-metric framework — peak adequacy, local modulation quality (PVDR<sub>local</sub>), and valley dose burden — over any single ratio.

This approach is scalable and reproducible, and could support SFRT optimization, plan comparison, and consistent reporting across institutions as SFRT use expands.

## CONCLUSIONS

Conventional peak-to-valley metrics derived from whole-GTV DVHs are insufficient to characterize SFRT plan quality.

Defining valley dose using anatomically meaningful, distance-based tumor subregions yields a local peak-to-valley ratio (PVDR<sub>local</sub>) that more directly reflects planner-controllable spatial dose modulation and better separates acceptable from suboptimal plans.

A structure-specific, multi-metric framework incorporating vertex coverage, PVDR<sub>local</sub>, and valley dose burden provides a practical, reproducible approach for guiding SFRT planning and evaluating plan quality across institutions.