RATS: A Framework for Robustness Comparison of IMPT and IMRT in Prostate DIL Lesion Boost Planning

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ABSTRACT

Purpose: To introduce and apply an analytically driven robustness evaluation framework, Robust Analysis Treatment Score (RATS), for systematic comparison of intensity-modulated proton therapy (IMPT) and intensity-modulated radiation therapy (IMRT) treatment plans for prostate cancer focal dominant intraprostatic lesion (DIL) boosts under clinically relevant geometric and range uncertainties.

Methods: Four prostate cancer patients were retrospectively replanned, generating twelve plans per patient using IMPT and IMRT, including nominal, robustly optimized, and geometrically expanded strategies. IMPT plans were evaluated across 39 combined geometric and range-uncertainty scenarios, while IMRT plans were evaluated across 19 geometric-perturbation scenarios. Dose-volume histogram data were extracted for targets and organs at risk and processed using a custom analysis workflow. Plan robustness was quantified using the RATS framework, which combines weighted uncertainty likelihood, organ-specific priority, constraint importance, and modeled tumor control and normal tissue complication probabilities into a composite score. To enable direct modality comparison, photon plan scores were normalized to account for the reduced number of evaluated uncertainty scenarios.

Results: Moderately robustly optimized proton plans consistently achieved the highest RATS values across all patients, outperforming nominal proton plans, geometrically expanded proton plans, and all photon plans in over 90 percent of evaluated uncertainty scenarios. Robust optimization yielded better preservation of target coverage and organ-at-risk sparing compared with margin-based expansion strategies. Photon plans exhibited a monotonic decline in robustness as geometric uncertainty increased. While interpatient variability was observed, robust IMPT plans maintained superior performance across diverse anatomical conditions.

Conclusion: RATS provides a quantitative, customizable framework for the assessment of treatment plan robustness under uncertainty. This study demonstrates that moderate robust optimization in IMPT yields superior robustness compared to geometric expansion approaches and IMRT for focal prostate DIL boosts. The framework shows strong potential for evaluating objective robustness and for comparative planning studies in advanced radiotherapy.

Key Finding

Moderate robust optimization produced the highest cohort-average RATS.

pG0R3	pG1R3	pPTV1
249%	235%	210%

Normalized to each patient's pG0R0 baseline (100%).
IMRT cohort averages ranged from 30.7% to -179%.

Study Design Summary

patients	plans	plan-scenario evaluations
4	48	1,552

IMPT: 39 uncertainty scenarios per plan
IMRT: 19 uncertainty scenarios per plan
Photon RATS scaled by 2.05 for scenario-count normalization

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INTRODUCTION & OBJECTIVE

Dominant intraprostatic lesions (DILs) are aggressive, often radioresistant regions of prostate cancer associated with an increased risk of local recurrence [1–4]. Focal dose escalation may improve tumor control but requires careful protection of nearby organs at risk [5]. Intensity-modulated proton therapy (IMPT) can reduce normal-tissue exposure through highly conformal dose delivery and minimal exit dose, but it is sensitive to range and setup uncertainties [6]. Intensity-modulated radiation therapy (IMRT) provides greater dosimetric stability but generally exposes more surrounding healthy tissue [7].

OBJECTIVE

To develop and evaluate the Robust Analysis Treatment Score (RATS), a flexible framework for comparing IMPT and IMRT plan robustness under clinically relevant uncertainties in prostate cancer patients receiving focal dose escalation to dominant intraprostatic lesions

METHODS & MATERIALS

Four patients with intermediate- to advanced-stage prostate cancer previously treated on the University of Miami UADAPT trial were retrospectively selected [8]. Each patient had received a 12–20 Gy focal boost to a dominant intraprostatic lesion using IMPT or IMRT.

All cases were replanned with a standardized 12 Gy DIL boost using both modalities. Plans incorporated different geometric margins and robust optimization settings (Table 1) while applying identical protocol-based dose constraints and optimization objectives. Treatment planning was performed in Eclipse v16 using Proton Convolution Superposition for IMPT and Acuros XB for IMRT dose calculation.

Table 1. Patient planning parameters for IMPT and IMRT. Patients were replanned to a standard 12 Gy boost (DIL) and normalized to target indicated below. Uncertainty parameters listed include: G- robustly calculated geometric expansions (mm); R- robustly calculated range uncertainty %; PTV isotropic geometric expansions of the DIL (mm). GTV = Gross Tumor Volume, PTV = Planning Target Volume, RO = Robust Optimization.

Plan Type	RO Constraints	Uncertainty Scenarios	Normalization Target Volume	Dose Coverage
$IMPT_{RO}$	V_{120_Gy}>95% DIL V_{12Gy}>35% GTV <4Gy to Rectum	G0R0 G0/R3.5% G1/R3.5% G3/R3.5% G5/R3.5%	GTV	V100% >95%
$IMPT_{PTV}$	N/A	PTV 1mm PTV 3mm PTV 5mm	PTV	V100% >95%
IMRT (12 Static-Fields)	N/A	PTV 0 PTV 1 mm PTV 3 mm PTV 5 mm	PTV	V100% >95%

Data Extraction and Analysis

For each patient, 12 IMPT and IMRT plans were generated and evaluated. Each IMPT plan included 39 geometric and range-uncertainty scenarios, while each IMRT plan included 19 geometric-uncertainty scenarios. DVH data from nominal and perturbed plans were extracted from Eclipse and analyzed using a custom Python script. Clinically relevant dose- and volume-based endpoints were assessed for target structures and organs at risk. Photon RATS values were multiplied by 2.05 to facilitate scenario-count-normalized comparison.

All patient-level normalized scores used pG0R0 = 100%.

Each plan was evaluated using a weighted algorithm informed by clinical priorities and published prostate SBRT TCP/NTCP models [9–10]. The RATS score combines uncertainty (U), constraint priority (C), organ importance (O), and TCP/NTCP probability (P) into a normalized metric that integrates target coverage and OAR sparing across uncertainty scenarios.

RATS SCORING FRAMEWORK

$$RATS = \sum_{i}^{n_C} \sum_{j}^{n_O} \sum_{k}^{n_U} C_{i,j}\, O_j U_k P_{i,j,k}$$

C	O	U	P
Constraint Score	Organ Score	Uncertainty Score	TCP / NTCP Score
Relative importance of each constraint within an organ or target volume	Clinical importance of each organ or structure in the treatment evaluation: GTV 6; rectum 5; bladder 4; lower-priority OARs 1-2	• Relative likelihood of each uncertainty scenario. • U scaled 0 to 1 • The higher the score, the more probable the clinical condition. Nominal 1.0 Range 0.9 G1/G3/G5 mm: 0.75/0.50/0.25	TCP for target control using Logistic Model (+ contribution) NTCP for normal-tissue risk using the LKB model [9-10] (- contribution) P Score scales from 0-1

DVH Endpoints

Targets: DIL/Lead12RT and GTV coverage / maximum dose.
OARs: bladder, rectum, urethra, body, femoral heads, and penile bulb.
Interpretation: Higher RATS indicates better preservation of target coverage and OAR sparing across perturbations.

RESULTS

Robustly optimized IMPT (pG0R3 and pG1R3) achieved the highest cohort-average normalized RATS.

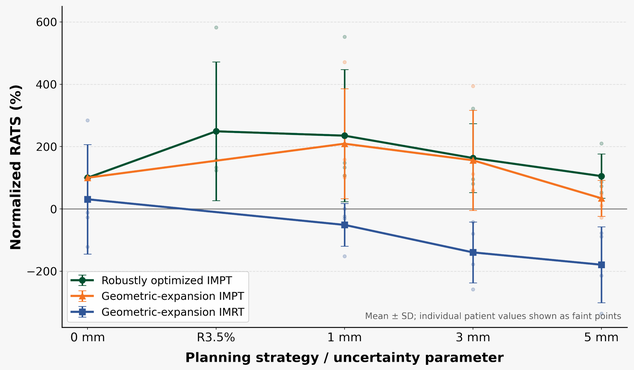

Figure 1. Cohort mean ± SD normalized RATS; faint points show individual patients. R3.5% denotes range uncertainty.

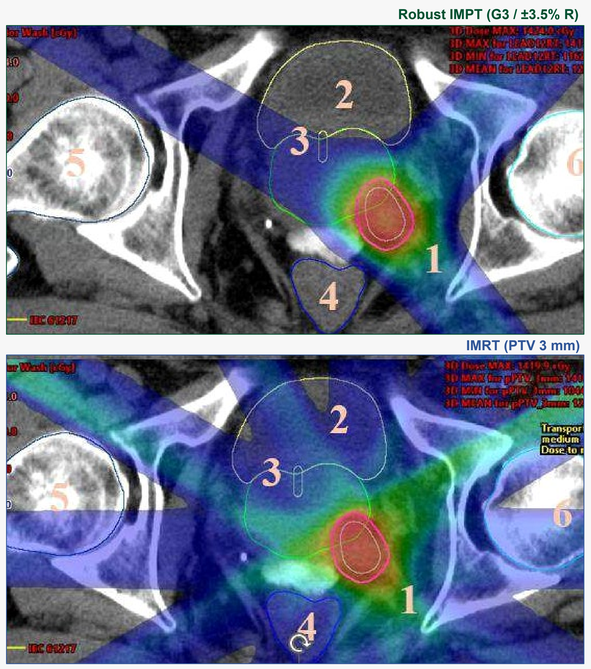

Figure 2. Isodose distribution for patient 1. (a) IMPT (G3R3.5) robustly optimized plan; G3 reflects 3mm geometric uncertainties, R3.5 reflects range uncertainties of ±3.5%. (b) IMRT (PTV3mm) optimized plan; PTV-3mm corresponds to a 3mm isotropic geometric expansion of GTV. Target (1) denotes the DIL encased by the PTV margin. The target is surrounded by several critical OARs: Bladder (2), Urethra (3), Rectum (4), Femoral Heads (5-6)

- Robustly optimized IMPT plans (pG0R3 and pG1R3) consistently achieved the highest RATS values across all patients.
- For Patient 1, pG0R3 and pG1R3 improved normalized RATS by approximately 20% relative to pG0R0; pPTV1 improved it by 4.5%.
- For Patients 2 and 3, pG0R3 and pG1R3 outperformed all other plans by at least 10%.
- For Patient 3, pG0R3, pG1R3, pG3R3, and pPTV1 improved RATS by more than 20%; pG0R3 and pPTV1 each achieved a score of approximately 90.
- Robust optimization generally outperformed geometric margin expansion, although pPTV1 remained competitive and exceeded all photon plans.
- Patient 4 showed the greatest variability, with a low baseline RATS of 10.4; nevertheless, pG0R3 and pG1R3 increased scores to 60.5 and 57.4, respectively.
- Across the cohort, average normalized RATS reached 249% for pG0R3 and 235% for pG1R3, compared with pG0R0 set to 100%.
- Geometrically expanded proton plans declined with increasing margin size, from 210% for pPTV1 to 34% for pPTV5.
- Photon plans consistently underperformed proton plans and worsened with larger margins, decreasing from 30.7% for PTV0 to −179% for PTV5.

COHORT-AVERAGE NORMALIZED RATS

pG0R3	pG1R3	pPTV1	PTV5
249%	235%	210%	-179%

Negative RATS values reflect the framework's penalty for unfavorable NTCP-weighted OAR performance; they are not probabilities.

DISCUSSION

- **RATS provides an integrated robustness assessment:** The framework combines dosimetric metrics, TCP/NTCP modeling, and clinically relevant weighting factors to objectively compare treatment plans while accounting for patient-specific anatomy and priorities.
- **Moderately robust IMPT plans performed best:** Proton plans using approximately 3 mm robust optimization, particularly pG0R3 and pG1R3, consistently achieved the highest RATS values across patients.
- **Robust optimization was superior to geometric margin expansion**: Directly incorporating setup and range uncertainties during optimization generally produced better target conformity and OAR sparing than compensating with isotropic PTV expansions.
- **Small geometric expansions may still be clinically useful:** The pPTV1 plans, using a 1 mm expansion, produced modest improvements in several patients, suggesting that minimized margins may be feasible when combined with appropriate robustness strategies.
- **Increasing margins generally reduced plan quality:** RATS scores progressively declined as geometric expansions increased, particularly because larger margins increased irradiation of normal tissues without providing equivalent robustness benefits.
- **IMPT consistently outperformed IMRT:** Proton plans maintained relatively high scores under uncertainty, whereas photon plans—especially those with larger expansions—frequently produced negative normalized RATS values.
- **TCP/NTCP modeling emphasized precise dose control:** The steep, sigmoidal dose-response relationships demonstrated the importance of maintaining target coverage while avoiding relatively small dose increases to high-priority OARs, particularly in hypo fractionated treatments.
- **Substantial interpatient variability was observed:** Differences in anatomy, planning configuration, and optimization quality strongly influenced RATS performance, supporting the use of individualized rather than exclusively population-averaged evaluations.
- **RATS may function as both a comparison and diagnostic tool**: High scores may identify favorable patient-specific planning configurations, while unexpectedly low scores may reveal optimization problems or degraded dosimetric quality.
- **Patient 4 represented an important anomaly:** Its low scores appeared more closely related to poor plan quality and elevated optimization cost-function values than to anatomical overlap, demonstrating the sensitivity of RATS to planning deficiencies.
- **Aggregate findings should be interpreted cautiously**: Although averaged results strongly favored moderately robust proton plans, the small four-patient cohort and wide score variability limit generalizability.

LIMITATIONS

- Small feasibility cohort (n=4) with substantial anatomical and dosimetric heterogeneity.
- Patient 4's low baseline inflated normalized ratios and cohort error bars.
- TCP/NTCP parameters, serial-organ assumptions, and priority weights were selected to demonstrate feasibility and require validation.
- The 2.05 photon scaling factor corrects scenario count but does not eliminate modality-specific modeling differences.

CONCLUSIONS

- RATS objectively evaluates plan robustness by combining dosimetric, TCP/NTCP, and clinical weighting factors.
- Moderately robust IMPT plans performed best, especially pG0R3 and pG1R3.
- Robust optimization was more effective than geometric margin expansion for maintaining coverage and sparing OARs.
- Small margins may be feasible, but larger expansions generally reduced plan quality.
- IMPT consistently outperformed IMRT, particularly under larger uncertainties.
- Patient anatomy and optimization quality strongly affected RATS scores, supporting individualized evaluation.
- RATS may identify both favorable planning strategies and suboptimal plans.
- Results support targeted robust optimization, although the small patient cohort limits generalizability

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Keywords: RATS = Robust Analysis Treatment Score | DIL = dominant intraprostatic lesion | IMPT = intensity-modulated proton therapy | IMRT = intensity-modulated radiation therapy