Evaluating Robustness of LET-Optimized Proton Therapy Pelvic Plans

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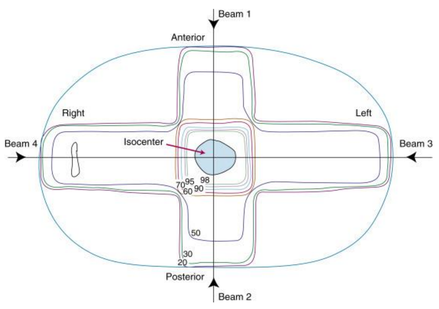
Introduction

Colorectal cancer is the third most diagnosed and second leading cause of cancer deaths in the United States.[1] Rising rates in younger adults have begun prompting screening beginning at age 45.[2,3] Anal cancer is rare in comparison to other gastrointestinal cancers, affecting only 1-2 people per 100,000, but its incidence is rising by 1-3% per year in developed countries. Symptoms may include bleeding, anorectal pain, or change in bowel habits. Risk is highest among individuals with HPV, those who are HIV-positive, and those with a history of receptive anal intercourse or with multiple sexual partners.[3] High-energy photons have traditionally been used for pelvic radiation; however, proton pencil-beam scanning has shown improved sparing of critical structures by using carefully selected beam arrangements to limit dose particularly to the bowel, bone marrow, and bladder.[4,7]



Robustness

Performing robustness evaluation involves simulating shifts anteriorly, posteriorly, superiorly, inferiorly, right, and left while accounting for density uncertainty.
The software generates sixteen scenarios depicting the possible altering of isodose distributions if patients were shifted at all during treatment setup. Robustness evaluation was performed for all beam sets.

Methods

Twenty patients treated with whole pelvis radiation therapy (WPRT) between 2016-2021 were included in this robustness study. Raystation pla nning software (version 12A, RaySearch Laboratories AB) was used for plan robustness calculations. Three beam configurations planned in an earlier study were chosen for evaluation.

- Beam arrangement 1 used three beams: two lateral-opposed and one anterior
- Beam arrangement 2 used three beams: two posterior oblique and one anterior
- Beam arrangement 3 used four beams: two lateral-opposed, one anterior and one posterior

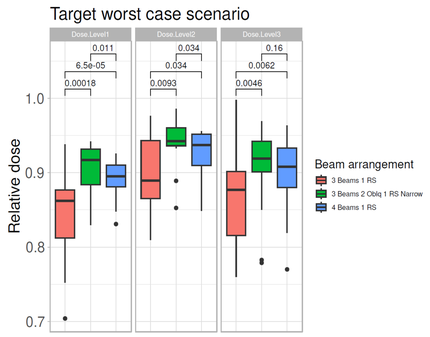
Results

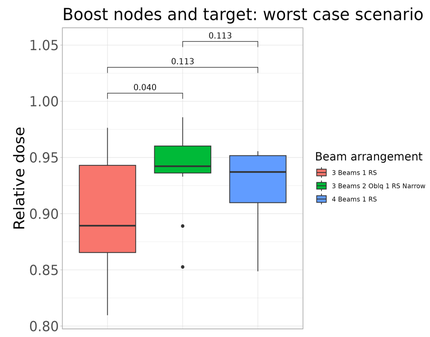
The goals and constraints were evaluated for:

- Targets: mean LET, nominal dose,
- Bladder: average and maximum dose
- Bone marrow: volumetric measurement: D90
- Genitalia: volumetric measurement: D20
- Bowel bag: maximum dose

Targets

- Differences between beam sets were relatively consistent between nominal plan dose and worst-case scenario doses
- Overall, differences in the dose to nodes and targets are not clinically relevant due to dose normalization to the targets when planning



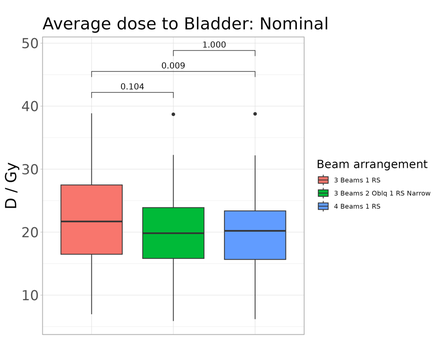


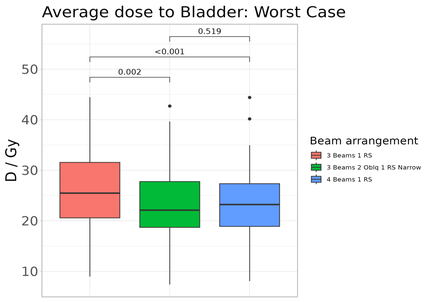
Organs at Risk (OARs)

- Difference in dose to genitalia had no clinical relevance between beam arrangements
- When evaluating bone marrow dose, Beam set 2 was the most robust plan and delivered the least dose
- Average and maximum dose to the bladder showed some significant difference between plans and this difference remained consistent for nominal and worst-case scenario doses
- Beam set 1 showed higher dose to bowel bag than Beam set 3 because it lacks a posterior beam to shift beam weighting from anterior

Table: Nominal dose statistics for bone marrow

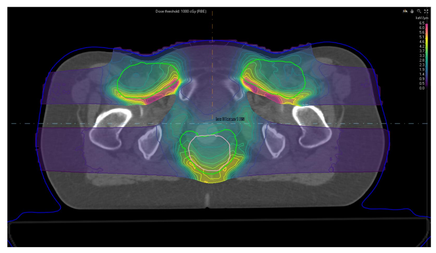
PlanType	Mean	SD	Median	N
3 Beams 1 RS	0.745	0.081	0.748	22
3 Beams 2 Oblq 1 RS Narrow	0.656	0.119	0.631	22
4 Beams 1 RS	0.740	0.121	0.784	22

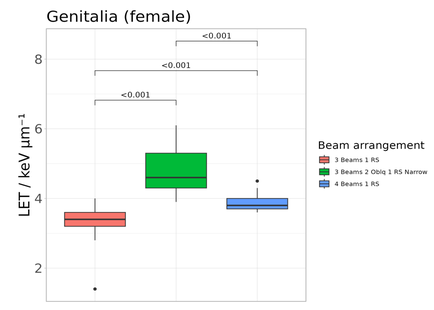


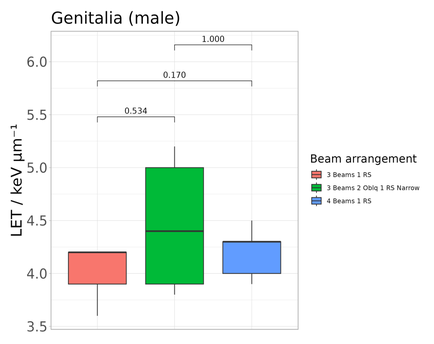


Linear Energy Transfer (LET)

- Beam set 1 shows significantly less LET in the targets that 2 or 3; it is uncertain if this results in clinical relevance
- Mean LET for female genitalia showed lowest LET for Beam set 1 and highest for Beam set 2
- Mean LET for male genitalia had no significant difference between beam sets







Limitations

- Small cohort and patient sex bias (17:5)
- No LET optimization due to older Raystation model
- Single choice of treatment couch: (posterior oblique beams affected)

Future Avenues of Study

- Conduct robustness test with verification CT scans (VSims) taken throughout patients' treatment course
- Use recent TPS models to perform LET-optimization on plans to find a metric which LET differences are clinically relevant

Conclusion

Although WPRT has been treated with lateral-opposed beams in the past to avoid dose to the bowel, Butala's study found that the most optimal arrangements utilize two anterior obliques and two posterior obliques. Beam set 2 most closely reflects these findings and addresses ways to avoid toxicities in the bowel bag and bone marrow. Decreasing low dose or entrance to the bone marrow may reduce the severity of hematologic toxicities.[14,15]

Acknowledgements

We'd like to thank Dr. Perles for his patience as we naviagated learning Raystation features and being a great research mentor all-round!

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