Penn Medicine

Proton Therapy for GYN Cancers: Evaluating Robustness of Different Beam Arrangements

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Proton Therapy for GYN Cancers

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Gynecologic Malignancies

- Second most common cancer site for women
- Approximately 100,000 new cases each year
- 60% of patients undergo radiation treatment as part of multi-modality treatment approach
  - Photon therapy is the primary treatment modality
  - More evidence is emerging supporting benefits of proton therapy

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Why Proton Therapy

- Reduced integral dose
- Lower bowel dose
- Improved bone marrow sparing – important when patients receive concurrent chemotherapy
  - Hematologic toxicity limits how much chemotherapy patient can receive
  - V10Gy and V20Gy – significant risk of developing acute hematologic toxicity
  - V40Gy – most predictive of toxicity

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Proton Therapy Challenges

- More sensitive to setup errors due to steep dose fall-off
  - Immobilization is very important
- Very sensitive to anatomy and density changes
  - Range uncertainty under variable bowel and rectal filling and presence of gas
  - Internal organ motion
  - Weight loss
- Robust optimization to counter these challenges

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Robust Optimization

- Optimize for solutions that don't fall apart with deviations from planning CT
  - Multiple uncertainty scenarios are accounted for during optimization
- In our clinic, standard uncertainty parameters are -
  - 5mm setup uncertainty
    - Patient positioning
    - Geometric alignment and field matching
  - 3.5% range uncertainty
    - Systematic uncertainty in the calculation of range
    - Change in path length due to bowel gas, bladder/rectal filling
    - Affects distal edge placement
- Beam arrangement can have a big impact on robustness

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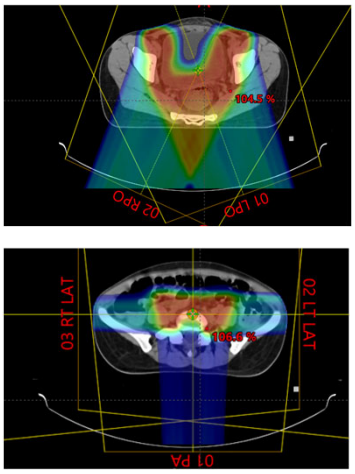
Beam Geometry

- "Ideal" beam angles
  - Stable anatomy/beam path
  - Fewest density changes
  - Distal edges are away from critical structures
- For this study, two different beam arrangements were evaluated
  - Posterior oblique beams, 20-25 degrees from PA
  - 3-beam technique: PA and two lateral beams



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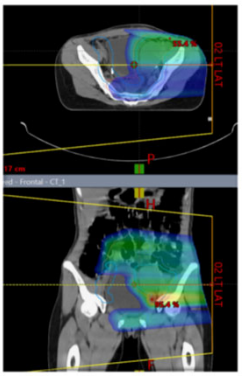
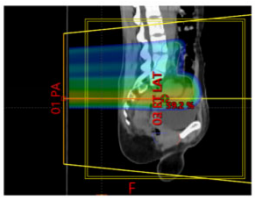
Field-specific targets for 3-beam arrangement

- Field-specific target volumes (FSTV)
  - Indicate where each beam is allowed to place spots
  - Improve robustness by avoiding placing a beam through highly variable areas
  - Help reduce dose to OAR by restricting a path through certain organs
- FSTV for this study
  - Inferior edge of PA field placed where nodal treatment volume starts
  - Primary volume treated with opposed lateral beams
  - Lateral beams restricted to treat ipsilateral nodes only
    - Do not cross bladder to the contralateral side
- Not every beam treats the entire target volume
  - Multi-field optimization technique is required





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SFO vs MFO

- Single-field optimization (SFO)
  - Equal contribution and uniform target coverage by each beam
  - Less sensitive to uncertainties
  - Theoretically, more robust because there is no interfiled dependency
- Multi-field optimization (MFO)
  - Better sparing of OAR
  - Improved conformality
  - More sensitive to uncertainties, maybe less robust

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Study Objectives

- Compare nominal dosimetry of each plan
- Determine if -
  - better nominal dosimetry translates into a more robust plan
  - or does conformality sacrifice robustness

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Methods & Materials

- Six patients
  - Simulated with full and empty bladder, planned on full bladder scan
- Two evaluation scans for each patient
- Planned on Eclipse TPS with robust optimization technique
- Prescription dose – 5040cGy in 28 fractions

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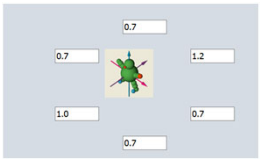
Target Volumes

- CTV_5040
  - iCTVp encompassing CTV from both full and empty bladder scans
  - Nodal CTV extending superiorly to about L3-4 interspace (CTVn)
- PTV expansion
  - 7mm from CTVn
  - Variable margin around iCTVp
    - Larger margin ant-post to account for variable bladder and rectal filling



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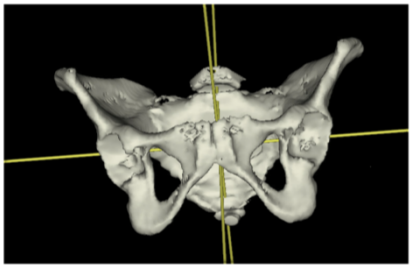
OAR & Planning Structures

- Rectum
- Bladder
- Bowel bag
- Femoral heads
- Pelvic bones



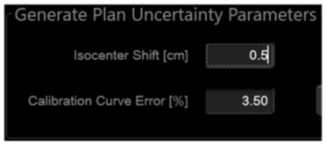
- Air and contrast with appropriate HU overrides
  - If no air override and bowel fills on treatment – range undershoot and target not covered
  - With air override and air present at treatment – range overshoot but target is still covered
- Plan appropriate planning structures, such as rectum-PTV

Planning Techniques

- Three plans for each patient, using robust optimization
  - 3 beams with MFO
  - 2 posterior obliques with MFO
  - 2 posterior obliques with SFO
- Range shifter used where appropriate
- Each plan optimized independently to optimal outcome

Optimization Parameters

- CTV_5040 optimized as a robust objective (RO)
  - Minimum and maximum robust objectives
- PTV included in optimization
  - RO only on maximum objective
- RO turned on for maximum doses for OAR
- Robust optimization perturbations – 5mm and 3.5%



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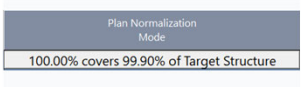
Target Evaluation Metrics

- CTV_5040 used as plan target for all plans
  - Normalized to same level of coverage for all plans
    - V100% @ 99.9%



- Other target metrics evaluated
  - CTV_5040 V98% and V95%
  - CTV_5040 D98% and D95%
  - PTV D97%
  - PTV D0.03cc

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OAR Evaluation Metrics

- Rectum
  - V40Gy (%)
  - D0.03cc (Gy)
- Bladder
  - V45Gy (%)
  - D0.03cc (Gy)
- Bowel bag
  - V30Gy (cc)
  - V40Gy (cc)
  - D0.03cc (Gy)
- Femoral heads
  - V30Gy (%)
  - D0.03cc (Gy)
- Pelvic bones
  - V10Gy (%)
  - V20Gy (%)
  - V40Gy (%)

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Nominal Plan Results

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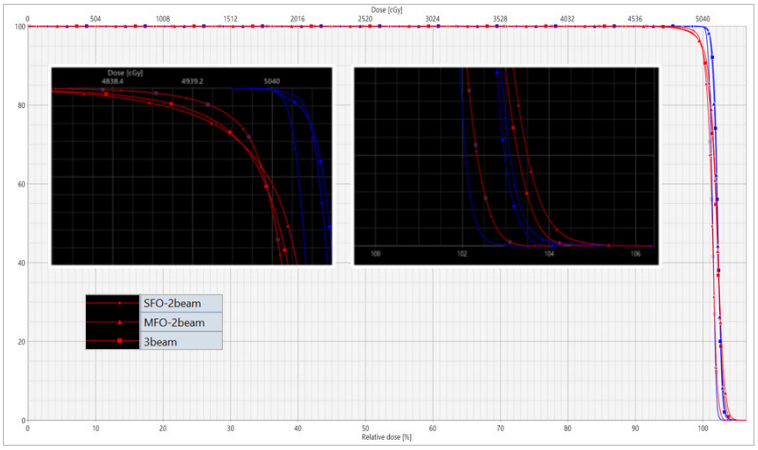
Nominal Plan Quality – Target Coverage

- All plans able to achieve V100% at 99.9% metric with reasonable hot spots
- All plans held up well under calculated plan uncertainties, maintaining V98%<99%



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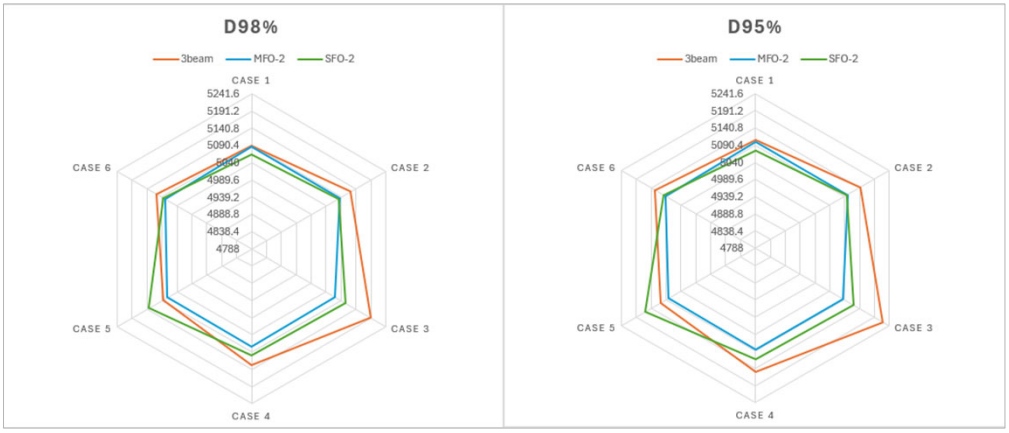
Nominal Plan Quality – CTV Coverage



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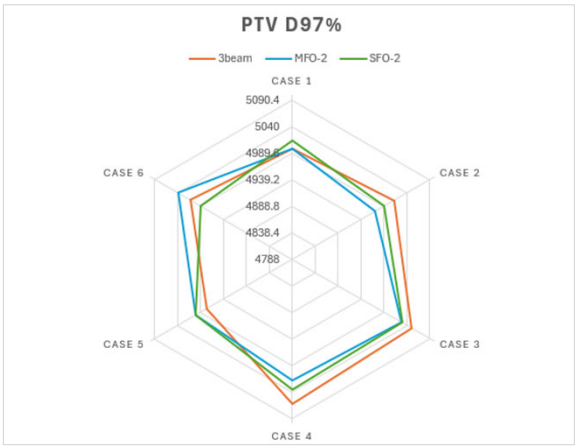
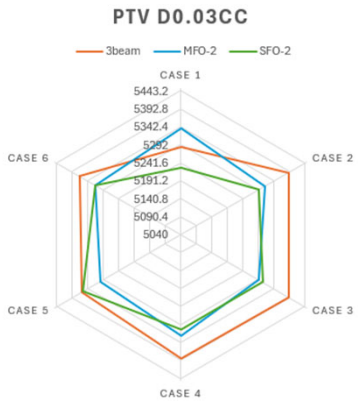
Nominal Plan Quality – PTV Coverage

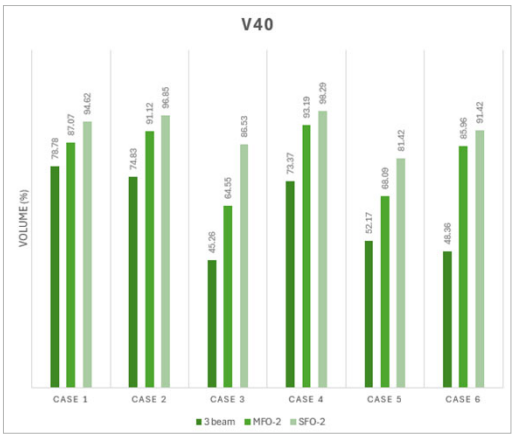


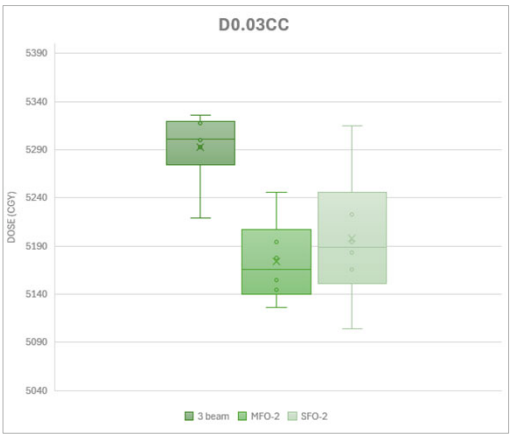
Nominal Plan Quality – Max dose

- Max doses are all within reasonable limits
- 3-beam plans are overall hotter to achieve the same level of normalization



OAR Sparing - Rectum





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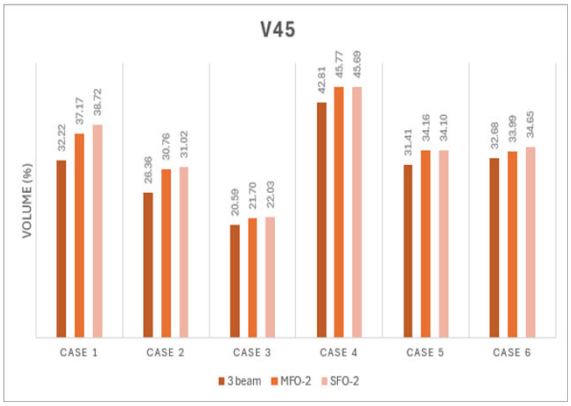
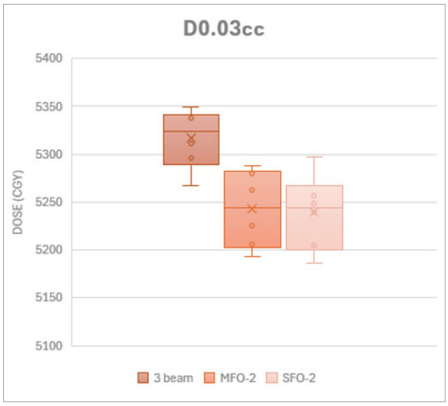
OAR Sparing - Bladder





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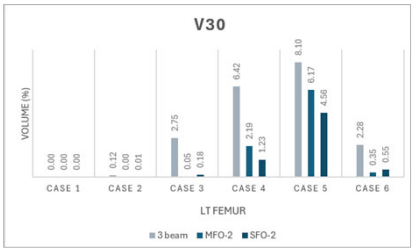
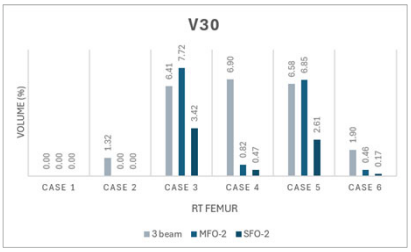
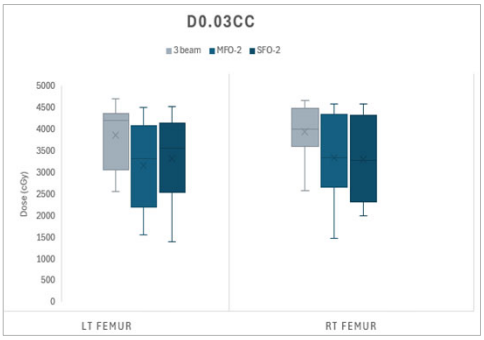
OAR Sparing – Femoral Heads





- Highly variable between each plan depending on proximity to treatment volume
  - Max dose range between 1500cGy and 4500cGy



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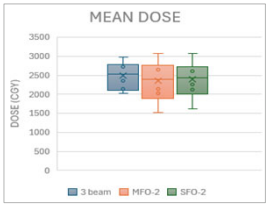
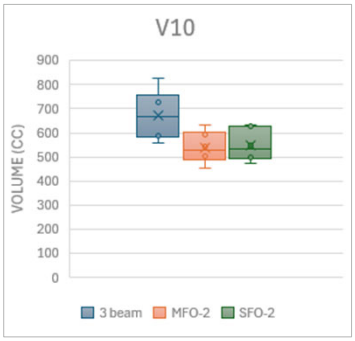
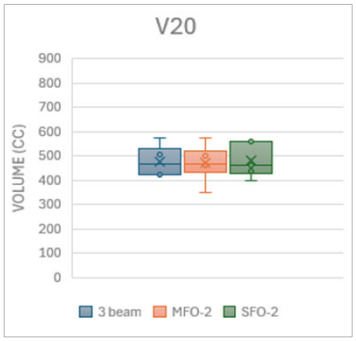
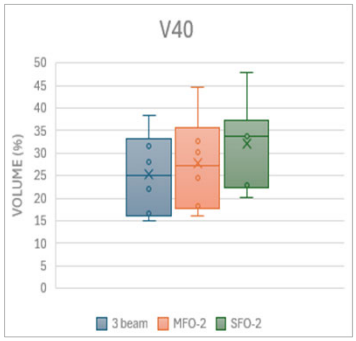
OAR Sparing – Pelvic Bone

- V10Gy – post oblique plans offer better sparing
- V20Gy – comparable across all plans
- V40Gy – less pelvic bone is exposed to 40Gy with a 3-beam technique









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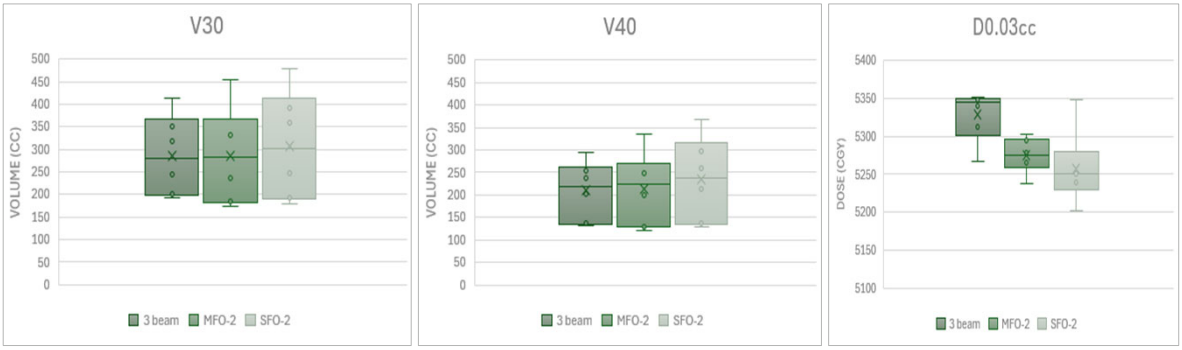
OAR Sparing – Bowel Bag

- Comparable across all plans



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Nominal Plan Results

- Good target coverage for all plans
- Plans look robust under normal perturbations
- 3-beam MFO plans tend to have higher max doses
  - Both for targets and OAR
  - Need to note that plan was normalized with V100% at 99.9%
    - Might not be clinically necessary

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Nominal Plan Results

- 3-beam MFO
  - Significantly lower rectal doses
    - FSTV to avoid placing PA beam through rectum
  - Slightly lower bladder doses
    - FSTV to avoid placing LAT beams through bladder
- For doses above 20Gy
  - 3-beam MFO is better for bowel bag and pelvic bones
- For doses above 20Gy
  - Post oblique beams are better
- Femoral heads received less dose with 2 post oblique beams

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Robustness Evaluation

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Reviewing Evaluation Scans

- Two scans for each patient were acquired during treatment
- Treatment volumes were transferred from the original CT
- OAR contoured independently for each scan
- Forward calculation of original plan with no air override on eval scan
- 12 data points to evaluate for each metric
  - % deviation from planning CT

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Robustness Results – CTV Target Coverage

- Evaluating mean % variation with standard deviation
- Lower SD = increased robustness

Metric	3 Beam MFO	2 Beam MFO	2 Beam SFO
V100 (%)	9.65 ± 3.33	8.63 ± 6.42	9.69 ± 6.91
V98 (%)	0.57 ± 0.55	2.17 ± 2.59	2.75 ± 3.74
V95 (%)	0.01 ± 0.02	0.47 ± 1.19	0.89 ± 1.88
D98 (%)	2.65 ± 0.64	2.62 ± 2.30	3.30 ± 2.59
D95 (%)	2.44 ± 0.60	1.81 ± 1.42	2.52 ± 1.93
PTV D97 (%)	3.05 ± 1.27	2.68 ± 1.92	3.14 ± 2.01
PTV D0.03cc (%)	3.21 ± 4.39	2.22 ± 2.72	0.97 ± 0.56

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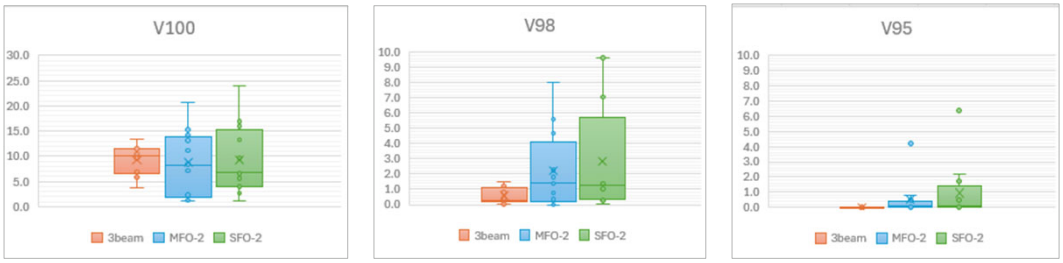
Target Volumes - Variation From Planning CT

- 3-beam plans appear more robust across all CTV metrics
  - V100% is not as clinically significant
- Some outliers in each category



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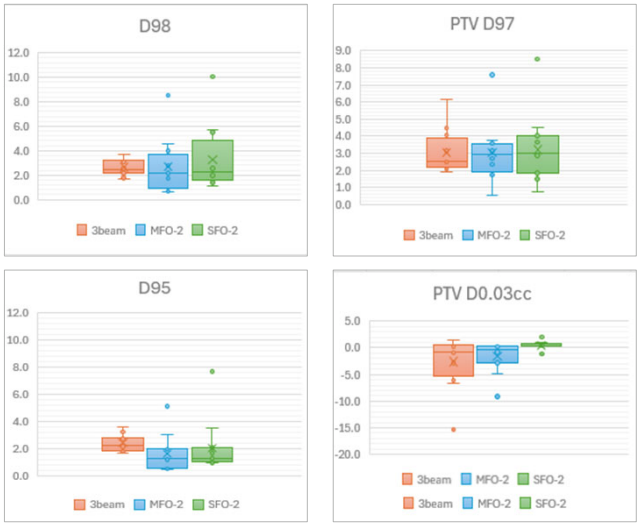
Target Volumes - Variation From Planning CT



- 3-beam MFO – varying robustness of PTV did not affect robustness of CTV
- Oblique SFO plans – excellent control of max dose

(+) dose lower than planning CT
(-) dose higher than planning CT

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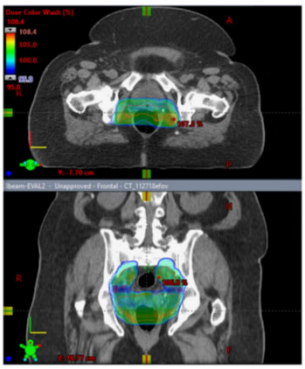
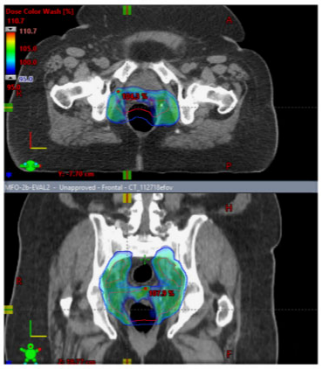
Evaluating Outliers – Excessive Air in Rectum

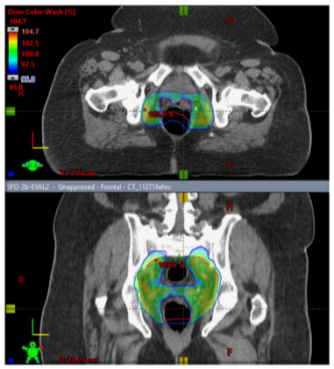
- Compromised robustness with posterior oblique beams
- 3-beam technique avoided placing PA beam through rectum



3 beam MFO w/FSTV



post oblique MFO



post oblique SFO

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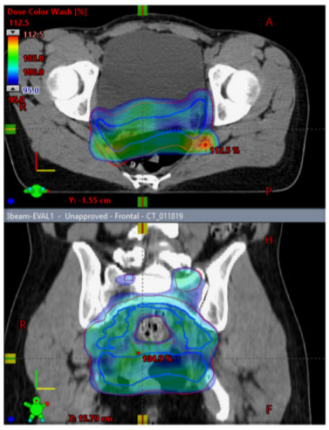
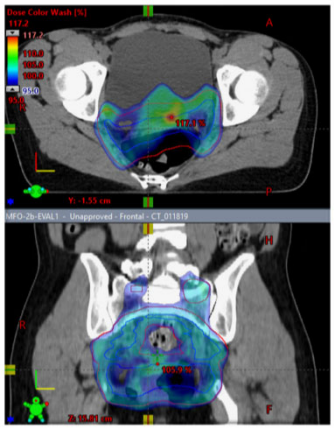
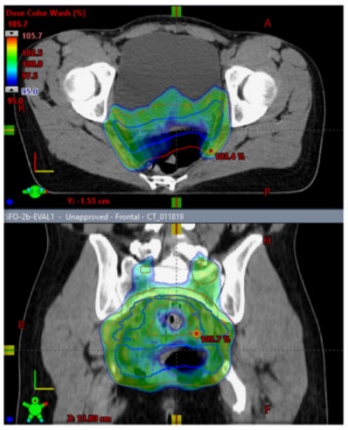
Evaluating Outliers – Excessive Air in Rectum



3 beam MFO w/FSTV



post oblique MFO



post oblique SFO

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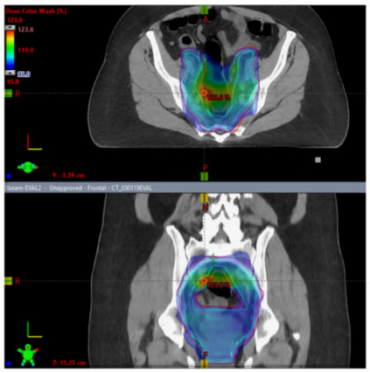
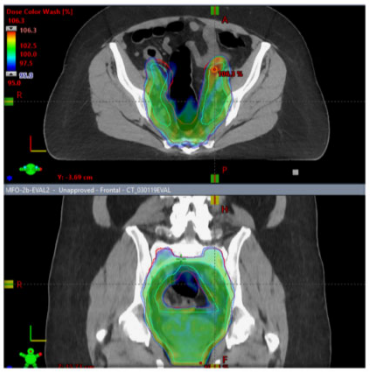
Max Dose Outlier

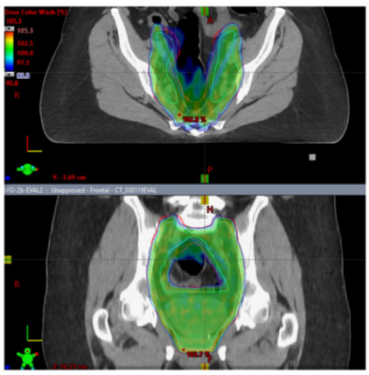
- Large volume of air in bowel in nodal region



3 beam MFO w/FSTV



post oblique MFO



post oblique SFO

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OAR Dose Deviation From Planning CT

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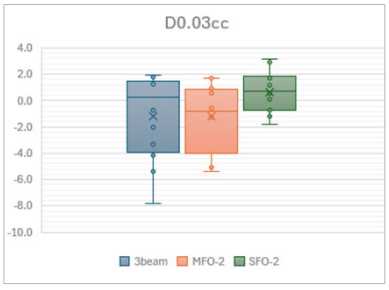
Robustness Results – OAR Sparing

Metric	3 Beam MFO	2 Beam MFO	2 Beam SFO
Rectum V40	24.7 ± 16.7	8.5 ± 5.3	5.5 ± 5.0
Rectum D0.03cc	2.69 ± 2.12	2.04 ± 1.91	1.39 ± 0.95
Bladder V45	25.2 ± 30.6	31.6 ± 44.4	30.6 ± 42.3
Bladder D0.03cc	1.75 ± 0.64	2.31 ± 3.09	0.94 ± 0.64
Bowel Bag V40	42.2 ± 31.8	46.1 ± 36.5	45.5 ± 31.8
Bowel Bag V30	36.3 ± 26.5	40.3 ± 30.7	38.8 ± 29.9
Bowel Bag D0.03cc	2.96 ± 4.10	0.44 ± 0.35	0.82 ± 0.76
Pelvic Bone V40	4.70 ± 2.90	2.76 ± 3.78	3.28 ± 3.15
Pelvic Bone V20	2.23 ± 1.32	1.33 ± 1.53	1.47 ± 1.37
Pelvic Bone V10	1.17 ± 1.01	1.45 ± 1.99	1.54 ± 1.92
Lt Femur D0.03cc	3.51 ± 3.42	7.22 ± 5.45	7.27 ± 6.17
Rt Femur D0.03cc	4.61 ± 3.50	9.52 ± 10.50	8.70 ± 9.43

- Evaluating mean % variation with standard deviation
- Most variability in rectal doses w/ 3-beam plans
- Large % deviation across all plans for bowel bag and bladder

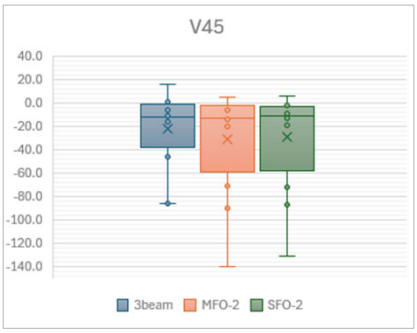
Rectum

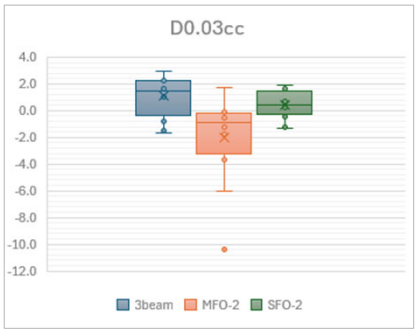
- Variation in rectal doses is greatest for a 3-beam technique
  - 4 plans – V40 lower than planning CT
  - 8 plans – V40 higher than planning CT
- Even with larger deviation from planning doses, irradiated rectal volume is still less than with post oblique techniques



Bladder

- In most cases bladder doses were higher than on planning CT





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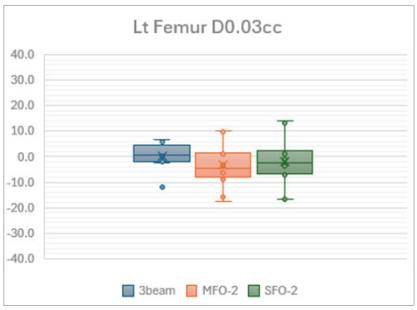
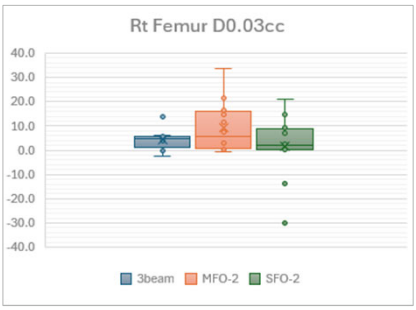
Femoral Heads





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Pelvic Bones

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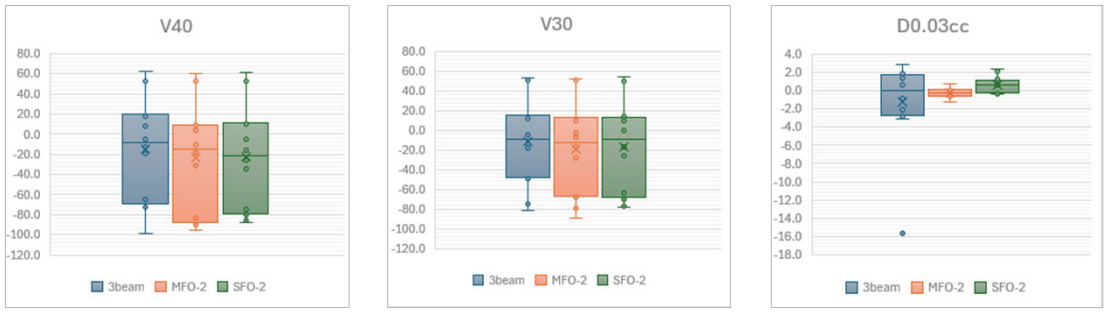
Bowel Bag



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Conclusion

- Although robust optimization helps with plan integrity, it cannot fully predict the extent of variation
  - Larger uncertainty margins would potentially increase dose to OAR
  - We compromise to achieve balance between target coverage and OAR sparing
- Generally, SFO optimization is thought to be less sensitive to uncertainties
  - All plans demonstrated the most degradation with SFO technique
    - Possibly because the uncertainty was centralized and affected both beams equally
- Improved nominal dosimetry of 3-beam MFO technique did not come at the expense of robustness

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Limitations

- Small sample size
- Only two evaluation scans per patient
- One planner experience

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Future Directions

- Larger patient cohort and more evaluation scans
- Curious to test more beam arrangements
  - Slightly off-lateral 3-field approach to see if pelvic bone doses can be lowered
  - 4-beam approach
    - Post oblique beams superiorly
    - Lateral or slightly off-lateral beams inferiorly

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