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Vaginal Sparing with Volumetric Modulated Arc Therapy (VMAT) for Rectal Cancer

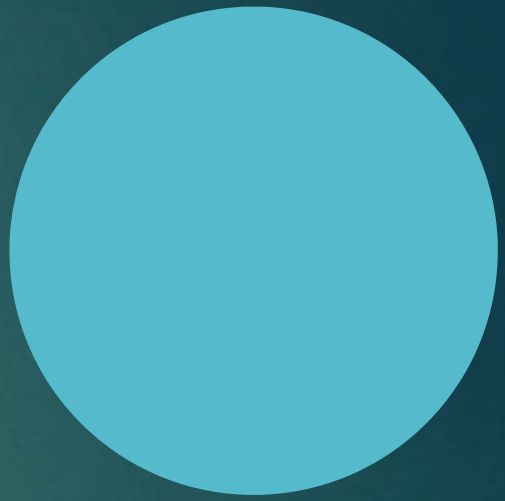
Scott Boulet BSc, RT(T)

Carolinas HealthCare System

Levine Cancer Institute

Outline

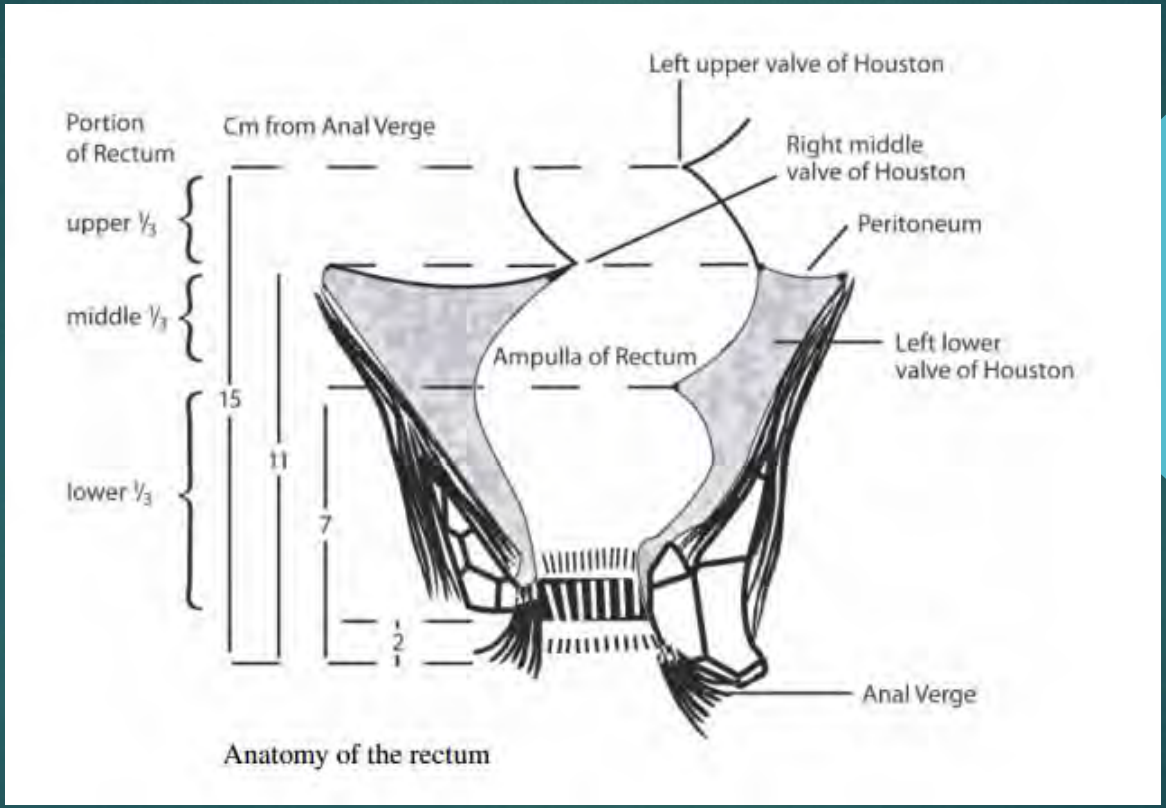
- Background
- Objectives
- Design
- Results
- Discussion
- Conclusion
- Acknowledgements
- Questions



Background

- RT for Rectal Cancer
- Anatomical considerations and challenges
- Vaginal side effects following RT
- Sexual Dysfunction: treatment and management
- Vaginal sparing: What is being done?
- Previous studies

Rectum Anatomy



Lu, J., & Brady, Luther W. (2010). *Decision Making in Radiation Oncology* (Medical Radiology Radiation Oncology). Dordrecht: Springer.

Rectal Cancer

AJCC TNM classification of rectal cancer (clinical or pathological)

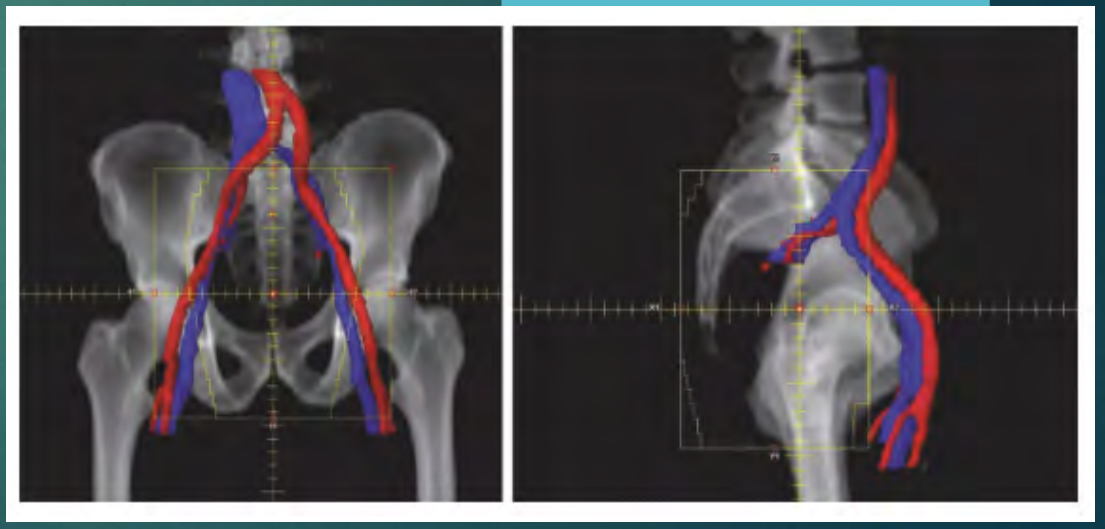
Stage	Description
Primary tumor (T)[a]	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ, intraepithelial or invasion of the lamina propria
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through the muscularis propria into perirectal tissue
T4a	Tumor penetrates to the surface of the visceral peritoneum
T4b	Tumor directly invades or is adherent to other organs or structures
Regional lymph nodes (N)[b]	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1a	Metastasis in 1 node
N1b	Metastasis in 2–3 regional nodes
N1c	Tumor deposits in the subserosa, mesentery, or nonperitonealized perirectal tissues without regional nodal metastasis
N2a	Metastasis in 4–6 regional nodes
N2b	Metastasis in 7 or more regional nodes
Distant metastasis (M)	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1a	Metastasis confined to one organ site (liver, lung, ovary, nonregional lymph node)
M1b	Metastases in more than one organ/site or the peritoneum

Lu, J., & Brady, Luther W. (2010). *Decision Making in Radiation Oncology* (Medical Radiology Radiation Oncology). Dordrecht: Springer.

Rectal Cancer

- 3D Conformal RT

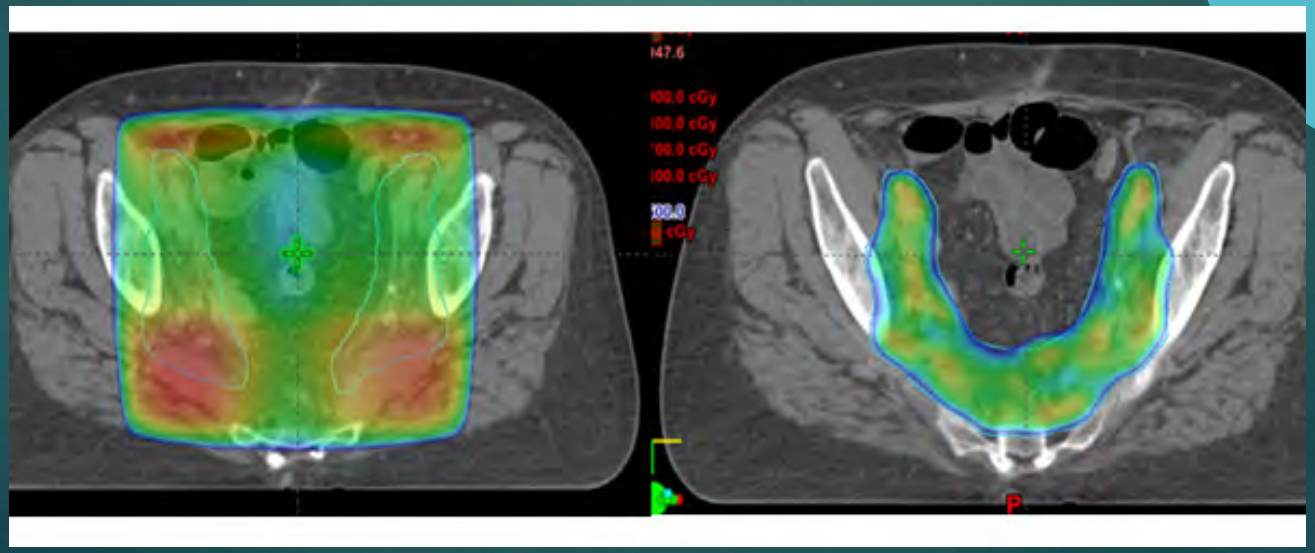
Fields	Borders
AP/PA or PA	■ Superior: between L5 and S1 ■ Inferior (in pre-op. setting): 3–5 cm below the palpable disease ■ Inferior (in post-op. setting): include perineum after APR or 2–3 cm beyond the anastomosis after LAR ■ Lateral: 1.5–2 cm lateral to the pelvic brim
Lateral	■ Superior/Inferior: as AP/PA fields ■ Anterior (T3 disease): 2- to 3-cm margin to the anterior of rectum or posterior margin of the pubic symphysis to cover internal iliac nodes (which ever is more anterior) ■ Anterior (T4 disease): 2- to 3-cm margin to the anterior of rectum or anterior margin of the pubic symphysis to cover external iliac nodes (which ever in more anterior) ■ Posterior: 1 cm behind the anterior edge of the sacrum, or many will include the entire sacrum
Boost	Gross tumor or tumor bed plus 3 cm in all directions



Lu, J., & Brady, Luther W. (2010). *Decision Making in Radiation Oncology* (Medical Radiology Radiation Oncology). Dordrecht: Springer.

Rectal Cancer IMRT

- Improved target coverage, homogeneity, and conformality, while lowering dose to adjacent organs-at-risk.
- The use of preoperative IMRT–IGRT with a SIB resulted in a high 5-year LC rate and non-negligible late toxicity

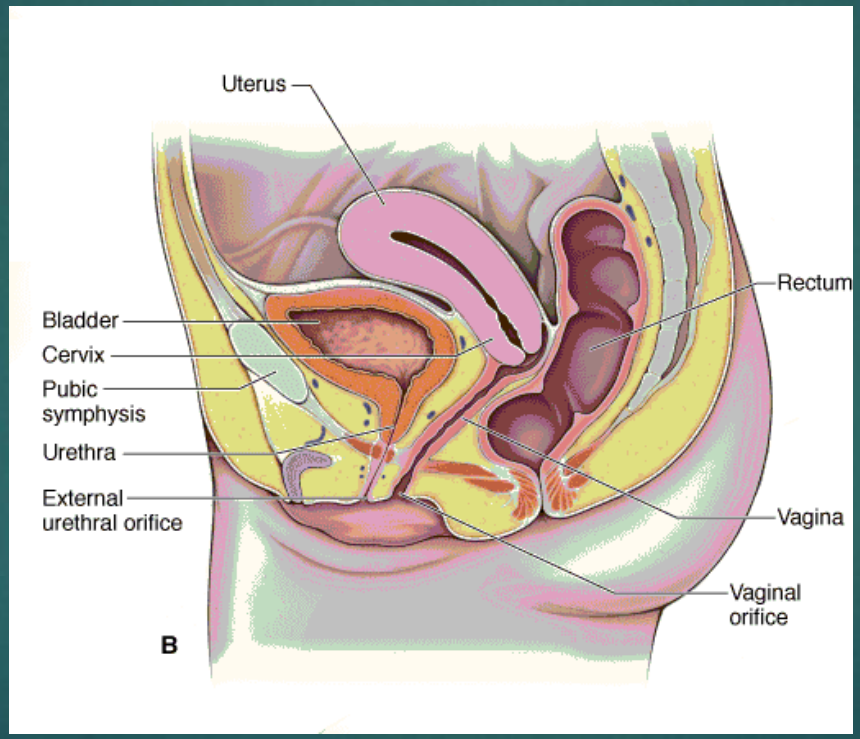


VMAT

- MLCs moving continuously as gantry rotates
- Delivering a sculpted, tightly-focused beam of radiation directly to a tumor in less than two minutes.

Varian Medical Systems ®

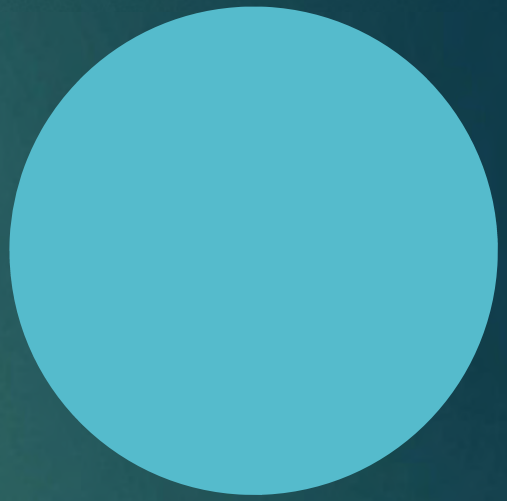
Female Pelvic Anatomy



Morton, D., Albertine, Kurt H., & Foreman, K. Bo. (2011). *The big picture gross anatomy* (McGraw-Hill's AccessMedicine). New York, N.Y.: McGraw Hill Medical.

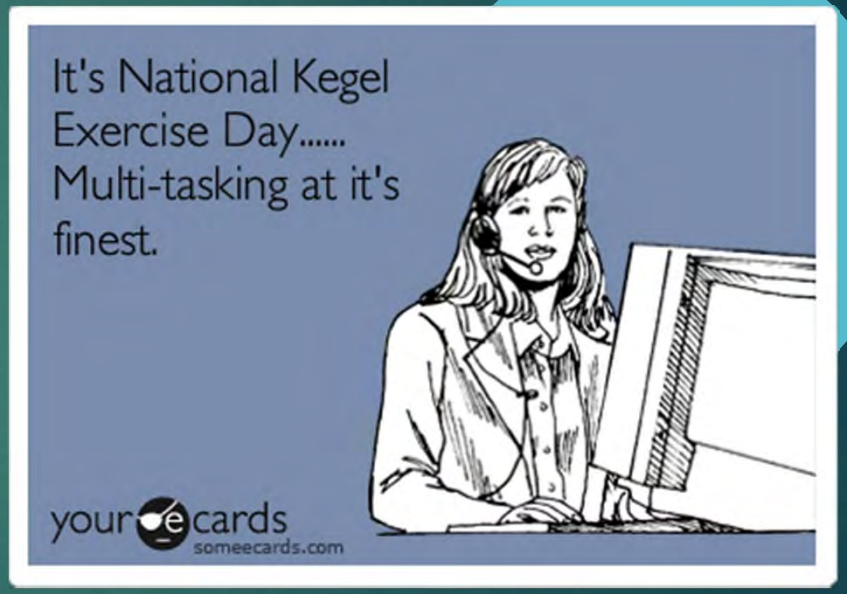
Vaginal Side Effects

- Sexual Dysfunction
- Dyspareunia
- Dryness
- Stenosis



Management Techniques

- Dilators
- Pelvic Floor Muscle training
- Lubricants
- Moisturizers
- Estrogen



Vaginal Dilators

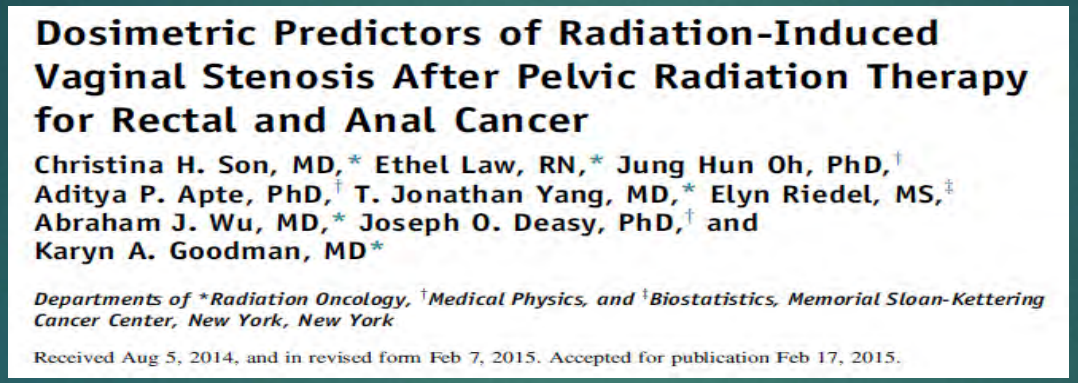
- includes the use of dilators, sexual intercourse, vibrators, fingers, or similar shaped devices
- commenced 2-8 weeks post radiotherapy,
- Risk of rectovaginal fistulae and psychological consequences
- Non-consistent education and compliance

Vaginal sparing: what is being done?

NOTHING! Why?

- Doesn't effect all people with rectal cancer
- Older women are less interested in sex
- Vagina is difficult to contour
- Not previously possible with 3DCRT
- Lack of literature
- Uncomfortable subject to talk about.

Vaginal sparing: what is being done?



Dosimetric Predictors of Radiation-Induced Vaginal Stenosis After Pelvic Radiation Therapy for Rectal and Anal Cancer

Christina H. Son, MD,* Ethel Law, RN,* Jung Hun Oh, PhD,† Aditya P. Apte, PhD,† T. Jonathan Yang, MD,* Elyn Riedel, MS,‡ Abraham J. Wu, MD,* Joseph O. Deasy, PhD,† and Karyn A. Goodman, MD*

*Departments of *Radiation Oncology, †Medical Physics, and ‡Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, New York*

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- As vaginal mean dose increases, vaginal stenosis increases.
- Severe vaginal stenosis is significantly reduced at mean doses <43Gy

Study Objectives

- To investigate whether VMAT treatment plans with, and without, vaginal sparing could significantly reduce the volume of the vagina that receives 20Gy (V20Gy), 30, 40, 45, or 50Gy when targeting rectal cancer tumours.
- Determine whether the maximum dose delivered, and the mean dose delivered are significantly different between the two treatment plans.

Methods

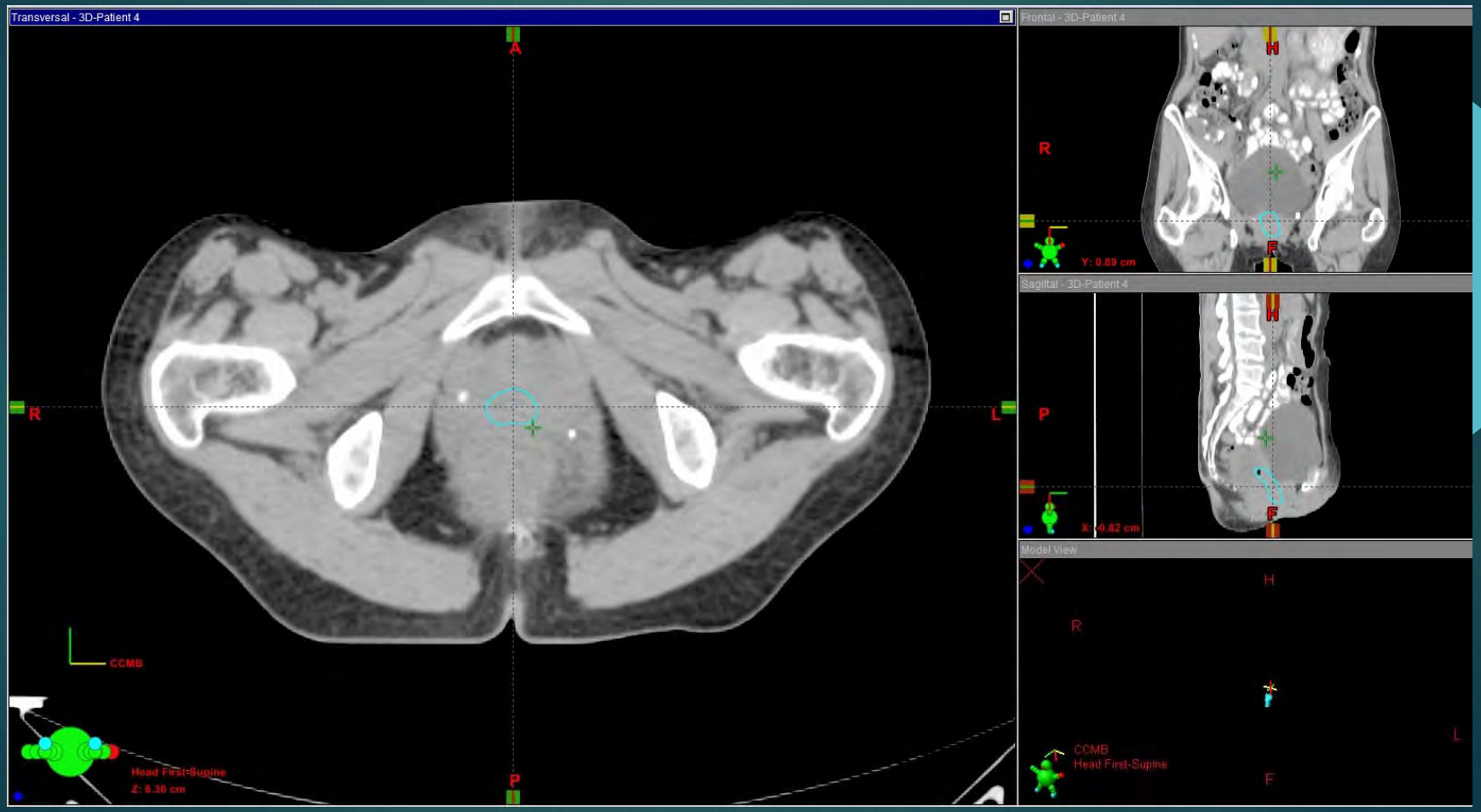
- Sample Size = 10 patients (Retrospective)
- Inclusion:

1) Diagnosed locally advanced rectal cancer
2) Stage T3, N1-2, MX/MO (Lower 1/3)
3) Recent pre-op MRI available for delineating the vagina
4) pre-operative 3DCRT At CancerCare Manitoba
5) 45G/25 FXs to the primary disease and lymph nodes, Boost 5.4Gy/3 FXs
6) simulated supine with full bladder and knee rest.

Contouring

- Vagina contoured by single physician
- Pre-op MRI used for delineating vagina
- Target volumes and OARs contoured as per RTOG Anorectal Atlas

Contouring


Transversal - 3D-Patient 4
A
R
L
P
CCMB
Head First-Supine
Z: 8.30 cm
Frontal - 3D-Patient 4
H
R
F
Y: 0.89 cm
Sagittal - 3D-Patient 4
H
P
F
X: -0.82 cm
Model View
H
R
L
F
CCMB
Head First-Supine

Contouring


Rotestpatient, Rovaginalsparing1 (T12300) - Contouring
Rotestpatient,...
T12300
No Current Activity
Worklist
Quicklinks
Khan, Junaid
Logout
File Edit View Insert Workspace Contouring Tools Window
Contouring
Registration
External Beam Planning
Brachytherapy Planning
Brachytherapy 2D Entry
Plan Evaluation
Selection
Contouring
NoSpare50.4_5
3D-Patient 4
Registered Images
MR Pt 4
REGISTRATION 3
Patient 4
Bladder 4
CouchInterior
CouchSurface
CTV45E 4
CTV50.4E 4
External 4
FemurLt 4
FemurRt 4
PTV45 4
PTV50.4 4
Small Bowel 4
Vagina 4
zCool2
zCool3
zPTV45 opt
Reference Points
DPV 50.4
DPV45 2
DPV45 4
DPV45 5
DPV45 Opt 3
DPV50.4 2
DPV50.4 3
DPV50.4 4
DPV50.4 5
PTV45
Verification
Verification1
User Origin
Transversal - 3D-Patient 4
Frontal - 3D-Patient 4
Sagittal - 3D-Patient 4
Model View
CCMB
Head First-Supine
Ready
User: jkhan
Group: RT Floor Sim
Site: Main
2:36 PM
9/1/2016

VMAT

- Two 360° coplanar arcs
- 6 MV
- Eclipse® V11 planning software(Varian Medical Systems)
- Rapid Arc® (VMAT)
- 2 phases 45GY/25 FXs, 5.4Gy/3FXs

Optimization

- Target coverage: D100% = 95% Rx, Dmax <107%
- OARs: Bladder, small bowel, femoral heads

<u>2VMAT Plans</u>

1) VMAT plan (normal)

- Goals: Target coverage, OARs ALARA

2) VMAT with vagina objective

- Goals: decrease vagina dose without compromising target coverage and OAR sparing.

Results

- Formal comparisons between the two treatment plans were carried using Wilcoxon signed-rank testing
- All data were available for analysis except the V20 and V30Gy volumes due to a lack of variability.
- Significant differences, even with the Bonferroni correction, were observed for the mean and maximum doses delivered, as well as for the V50Gy volumes.
- The V45Gy volumes also appeared different between the two treatment plans (Table 2) and would normally be considered significant at the *P*-value≤0.05 threshold, but because the threshold *P*-value was adjusted using the Bonferroni correction, it was no longer significant.

Results

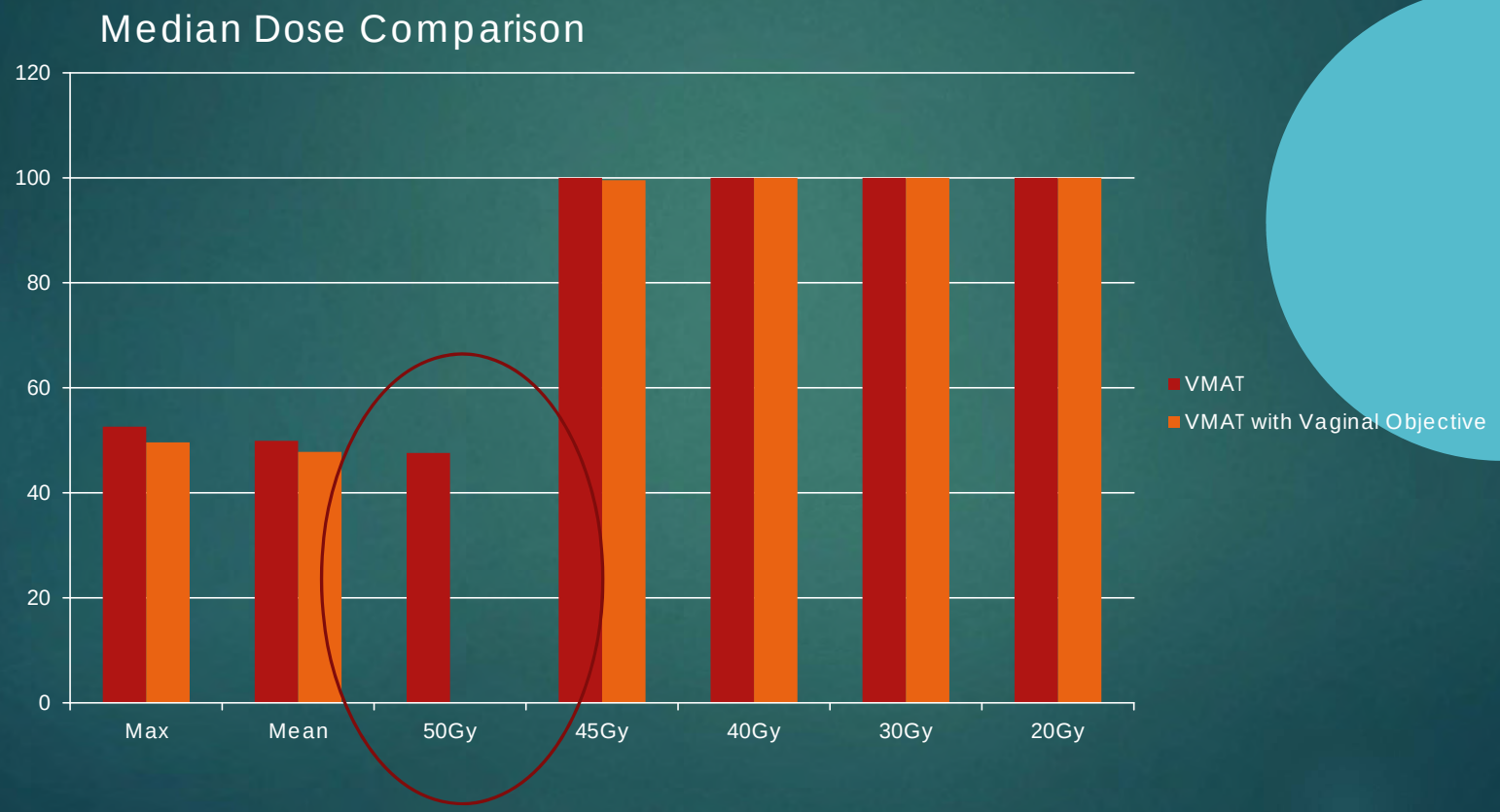

Median Dose Comparison
120
100
80
60
40
20
0
Max
Mean
50Gy
45Gy
40Gy
30Gy
20Gy
VMAT
VMAT with Vaginal Objective

Table 1: Descriptive statistics of mean and maximum doses delivered by each of the VMAT treatment plans.

Results

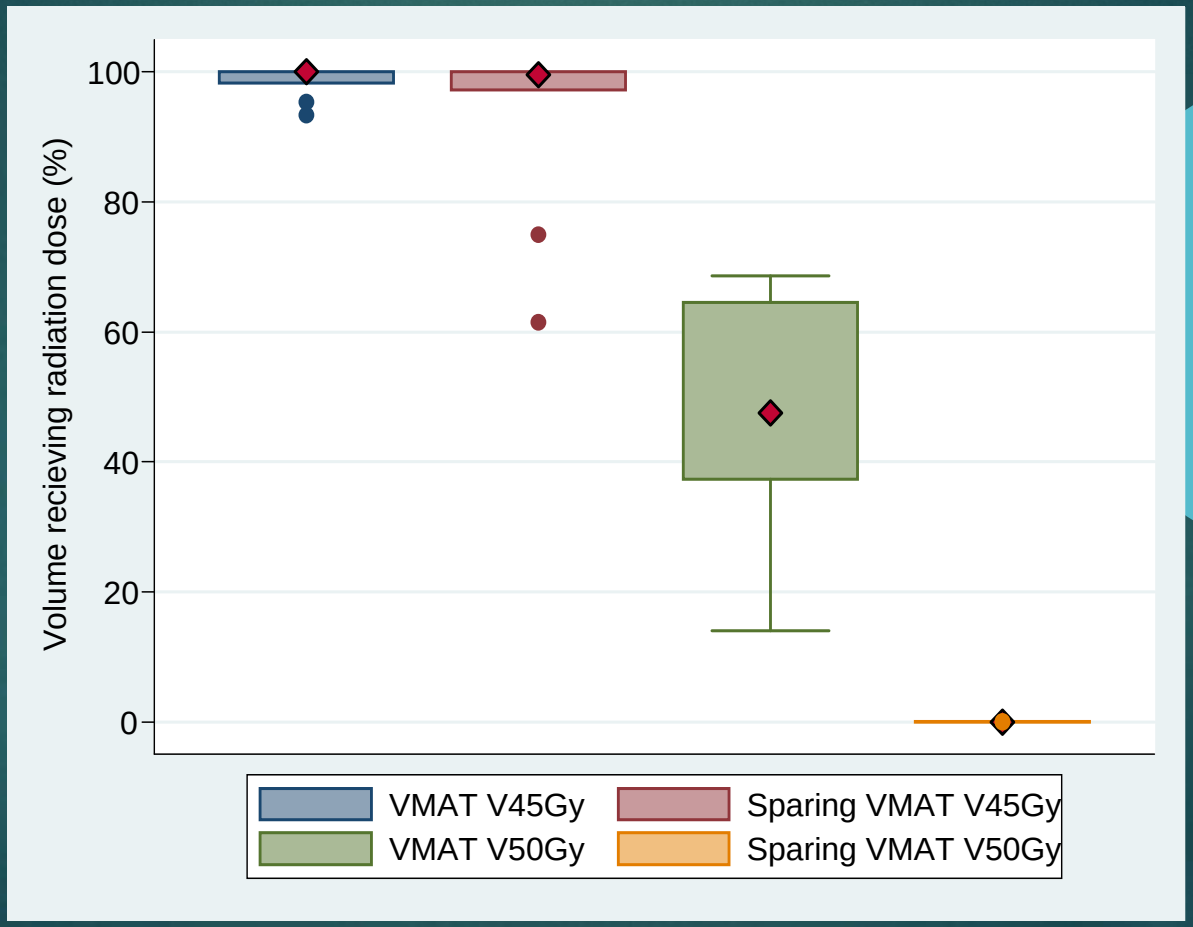
Variable	Median	IQR	90th percentile	Minimum	Maximum
VMAT					
Mean Dose (cGy)	4990.90	71.60	5044.80	4779.20	5048.90
Maximum Dose (cGy)	5255.85	44.40	5314.60	5150.50	5319.40
VMAT with vaginal sparing					
Mean Dose (cGy)	4779.50	130.4	4876.00	4654.20	4880.20
Maximum Dose (cGy)	4962.80	65.20	5022.35	4922.3	5025.20

Table 2: Frequency and percent of volumes of the vagina exposed to 20, 30 40, 45 or 50Gy by each of the two VMAT treatment plans.

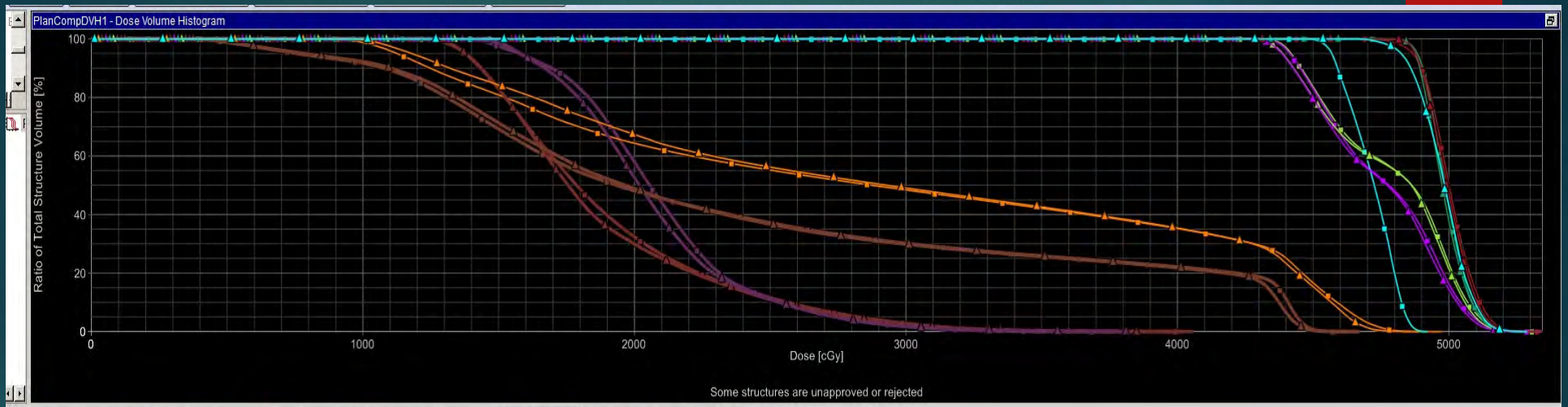
Results

VMAT				VMAT with vaginal sparing		
Values	Frequency	Percent		Values	Frequency	Percent
V20Gy				V20Gy		
100.00	10	100.00		100.00	10	100.00
V30Gy				V30Gy		
100.00	10	100.00		100.00	10	100.00
V40Gy				V40Gy		
99.20	1	10.00		96.90	1	10.00
100.00	9	90.00		99.10	1	10.00
				100.00	8	80.00
V45Gy						
93.30	1	10.00		V45Gy		
95.30	1	10.00		61.50	1	10.00
98.20	1	10.00		74.90	1	10.00
99.80	1	10.00		97.20	1	10.00
100.00	6	60.00		98.20	1	10.00
				99.30	1	10.00
V50Gy				99.80	1	10.00
14.00	1	10.00		100.00	4	40.00
36.60	1	10.00				
37.30	1	10.00		V50Gy		
43.30	1	10.00		0.00	7	70.00
46.90	1	10.00		0.01	1	10.00
48.20	1	10.00		0.03	1	10.00
60.10	1	10.00		0.10	1	10.00
64.50	1	10.00				
67.40	1	10.00				
68.60	1	10.00				

Results


Volume recieving radiation dose (%)
100
80
60
40
20
0
VMAT V45Gy
Sparing VMAT V45Gy
VMAT V50Gy
Sparing VMAT V50Gy

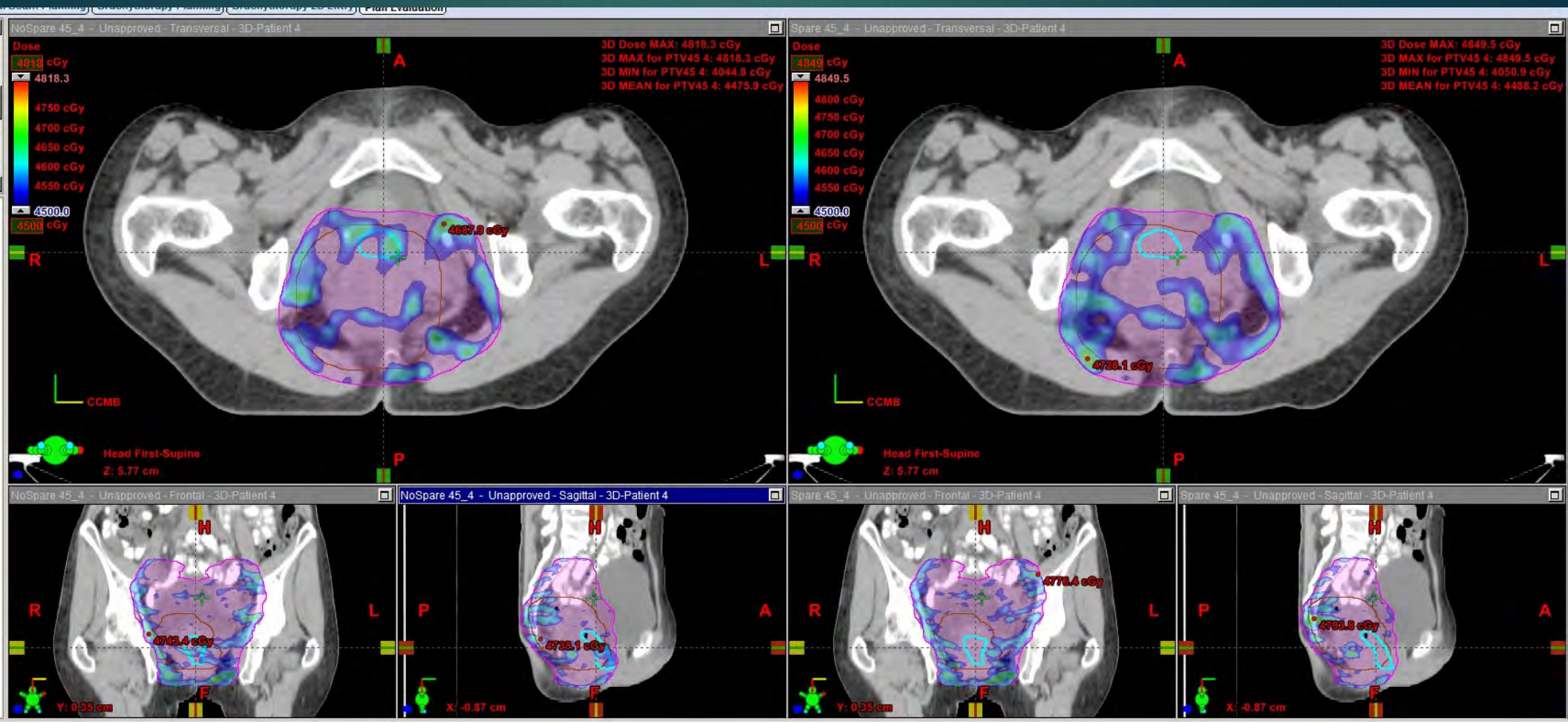
DVH Comparison



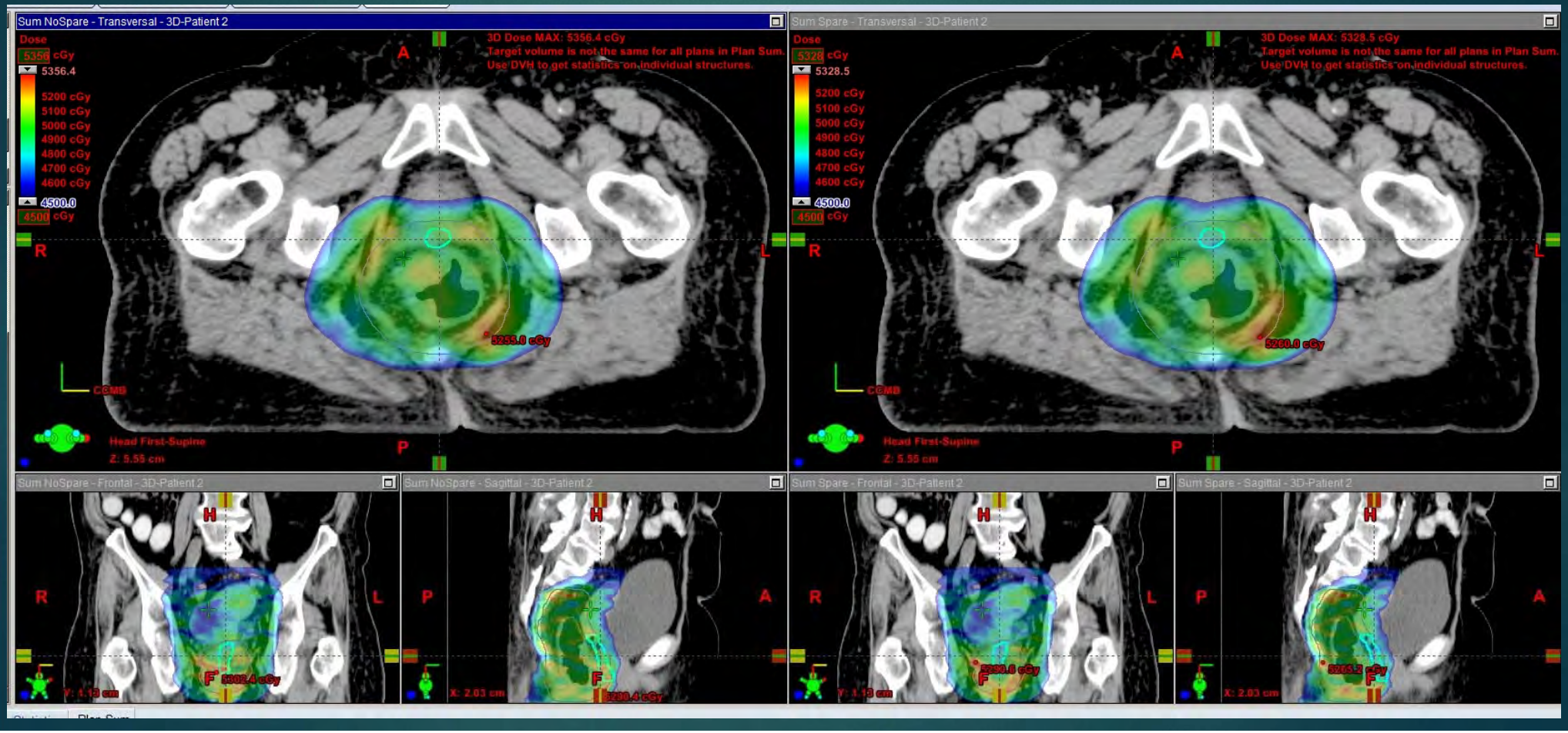
Fields | Dose Prescription | Field Alignments | Plan Objectives | Optimization Objectives | Dose Statistics | Calculation Models | Plan Sum

View	DVH Line	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [cGy]	Max Dose [cGy]	Mean Dose [cGy]
☑		Bladder 3	Approved	Sum Spare	Patient 3	236.2	100.0	100.0	900.2	4977.7	2952.4
☑		Bladder 3	Approved	Sum NoSpare_3	Patient 3	236.2	100.0	100.0	921.8	4889.1	2993.1
☑		CTV45E 3	Approved	Sum Spare	Patient 3	828.8	100.0	100.0	4264.0	5338.4	4791.4
☑		CTV45E 3	Approved	Sum NoSpare_3	Patient 3	828.8	100.0	100.0	4196.9	5344.6	4777.1
☑		CTV50.4E 3	Approved	Sum Spare	Patient 3	120.5	100.0	100.0	4738.5	5320.1	4990.7
☑		CTV50.4E 3	Approved	Sum NoSpare_3	Patient 3	120.5	100.0	100.0	4764.1	5344.6	4982.1
☐		External 3	Approved	Sum Spare	Patient 3						
☐		External 3	Approved	Sum NoSpare_3	Patient 3						
☑		FemurLt 3	Approved	Sum Spare	Patient 3	134.1	100.0	100.0	1325.7	3787.9	2092.5
☑		FemurLt 3	Approved	Sum NoSpare_3	Patient 3	134.1	100.0	100.0	1347.4	3816.3	2066.1
☑		FemurRt 3	Approved	Sum Spare	Patient 3	137.5	100.0	100.0	1197.7	4016.8	1900.5
☑		FemurRt 3	Approved	Sum NoSpare_3	Patient 3	137.5	100.0	100.0	1238.8	4063.6	1881.5
☑		PTV45 3	Approved	Sum Spare	Patient 3	1598.5	100.0	100.0	4041.2	5338.4	4757.2
☑		PTV45 3	Approved	Sum NoSpare_3	Patient 3	1598.5	100.0	100.0	4089.2	5344.6	4741.2
☐		PTV45 Opt 3	Approved	Sum Spare	Patient 3						
☐		PTV45 Opt 3	Approved	Sum NoSpare_3	Patient 3						
☑		PTV50.4 3	Approved	Sum Spare	Patient 3	338.7	100.0	100.0	4663.8	5338.4	5003.7
☑		PTV50.4 3	Approved	Sum NoSpare_3	Patient 3	338.7	100.0	100.0	4714.1	5344.6	4997.3
☑		Small Bowel 3	Approved	Sum Spare	Patient 3	320.8	100.0	100.0	364.5	4675.3	2393.7
☑		Small Bowel 3	Approved	Sum NoSpare_3	Patient 3	320.8	100.0	100.0	363.5	4668.9	2399.0
☑		Vagina 3	Unapproved	Sum Spare	Patient 3	18.3	100.0	99.9	4455.5	4922.3	4715.8
☑		Vagina 3	Unapproved	Sum NoSpare_3	Patient 3	18.3	100.0	99.9	4612.7	5290.7	4979.2

Phase 1: 45 Gy


NoSpare 45_4 - Unapproved - Transversal - 3D-Patient 4
Dose
4818 cGy
4818.3
4750 cGy
4700 cGy
4650 cGy
4600 cGy
4550 cGy
4500.0
4500 cGy
3D Dose MAX: 4818.3 cGy
3D MAX for PTV45 4: 4818.3 cGy
3D MIN for PTV45 4: 4044.8 cGy
3D MEAN for PTV45 4: 4475.9 cGy
4687.9 cGy
A
R
L
P
CCMB
Head First-Supine
Z: 5.77 cm
Spare 45_4 - Unapproved - Transversal - 3D-Patient 4
Dose
4849 cGy
4849.5
4800 cGy
4750 cGy
4700 cGy
4650 cGy
4600 cGy
4550 cGy
4500.0
4500 cGy
3D Dose MAX: 4849.5 cGy
3D MAX for PTV45 4: 4849.5 cGy
3D MIN for PTV45 4: 4050.9 cGy
3D MEAN for PTV45 4: 4488.2 cGy
4728.1 cGy
A
R
L
P
CCMB
Head First-Supine
Z: 5.77 cm
NoSpare 45_4 - Unapproved - Frontal - 3D-Patient 4
H
R
L
F
4743.4 cGy
Y: 0.35 cm
NoSpare 45_4 - Unapproved - Sagittal - 3D-Patient 4
H
P
A
F
4738.1 cGy
X: -0.87 cm
Spare 45_4 - Unapproved - Frontal - 3D-Patient 4
H
R
L
F
4778.4 cGy
Y: 0.35 cm
Spare 45_4 - Unapproved - Sagittal - 3D-Patient 4
H
P
A
F
4783.8 cGy
X: -0.87 cm

Plan Sum: 50.4 Gy/28Fx



Discussion

- Significance of decreasing the V50Gy, mean and maximum doses
- Contouring
- Vaginal Motion
- Use of a dilator during RT
- IGRTs role in vaginal sparing
- Concerns

reducing the V50Gy, mean, and maximum dose

- Does Vaginal Sparing translate to decreased toxicity?

Dosimetric Predictors of Radiation-Induced Vaginal Stenosis After Pelvic Radiation Therapy for Rectal and Anal Cancer

Christina H. Son, MD,* Ethel Law, RN,* Jung Hun Oh, PhD,† Aditya P. Apte, PhD,† T. Jonathan Yang, MD,* Elyn Riedel, MS,‡ Abraham J. Wu, MD,* Joseph O. Deasy, PhD,† and Karyn A. Goodman, MD*

*Departments of *Radiation Oncology, †Medical Physics, and ‡Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, New York*

Received Aug 5, 2014, and in revised form Feb 7, 2015. Accepted for publication Feb 17, 2015.

Purpose: Although vaginal stenosis (VS) is a recognized toxicity in women who receive pelvic radiation therapy (RT), the relationship between RT dose and the volume and extent of toxicity has not been analyzed. We modeled this relationship to identify predictors of VS.

Methods and Materials: We evaluated 54 women, aged 29 to 78 years, who underwent pelvic RT for rectal or anal cancer during 2008 to 2011 and were enrolled in a prospective study evaluating vaginal dilator use. Maximum dilator size was measured before RT (baseline) and 1 month and 12 months after RT. Dilator use was initiated at 1 month. The difference (D) in dilator size before and after RT was recorded. Those with $D \leq -1$ were classified as having VS (n = 35); those with $D \geq 0$ were classified as having no VS (n = 19 at 1 month). Dose-volume parameters were extracted, and the generalized equivalent uniform dose (gEUD) was used to build a predictive model.

Results: The mean vaginal doses were 50.0 Gy and 36.8 Gy for anal and rectal cancer patients, respectively. One month after RT, a gEUD model using a wide range of a values suggests that sparing of vaginal volume to a low dose may be important. When gEUD ($a = -1$) was <35 Gy and the mean vaginal dose was <43 Gy, severe VS was reduced ($P = .02$). A 1-year analysis suggests increasingly negative D values with increasing mean dose. However, patients with compliance <40% were more likely to have toxicity.

Conclusions: Vaginal stenosis is influenced by multiple RT dose-volume characteristics. Mean dose and gEUD constraints together may reduce the risk of severe VS.

Vaginal Motion

VAGINAL MOTION AND BLADDER AND RECTAL VOLUMES DURING PELVIC INTENSITY-MODULATED RADIATION THERAPY AFTER HYSTERECTOMY

ANUJA JHINGRAN, M.D.,* MOHAMMAD SALEHPOUR, PH.D.,† MARIANNE SAM, B.S.,* LARRY LEVY, M.S.,* AND PATRICIA J. EIFEL, M.D.*

Departments of *Radiation Oncology and †Radiation Physics, The University of Texas M. D. Anderson Cancer Center, Houston, TX

Purpose: To evaluate variations in bladder and rectal volume and the position of the vaginal vault during a 5-week course of pelvic intensity-modulated radiation therapy (IMRT) after hysterectomy.

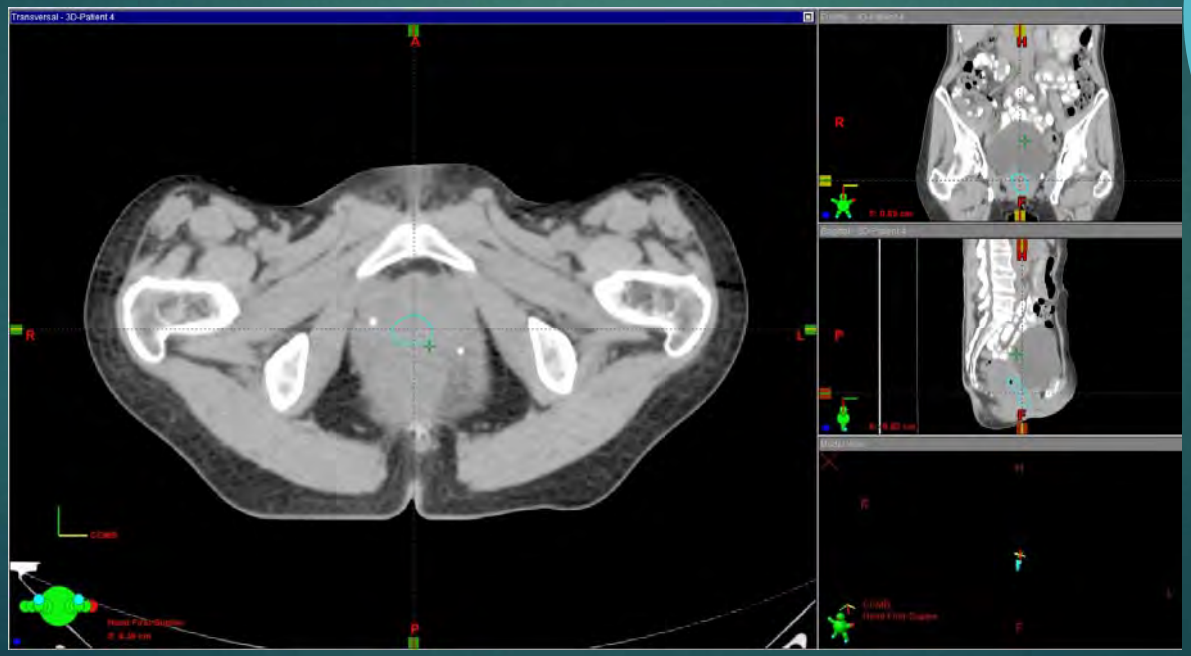
Methods and Materials: Twenty-four patients were instructed how to fill their bladders before simulation and treatment. These patients underwent computed tomography simulations with full and empty bladders and then underwent rescanning twice weekly during IMRT; patients were asked to have full bladder for treatment. Bladder and rectal volumes and the positions of vaginal fiducial markers were determined, and changes in volume and position were calculated.

Results: The mean full and empty bladder volumes at simulation were 480 cc (range, 122–1,052) and 155 cc (range, 49–371), respectively. Bladder volumes varied widely during IMRT: the median difference between the maximum and minimum volumes was 247 cc (range, 96–585). Variations in rectal volume during IMRT were less pronounced. For the 16 patients with vaginal fiducial markers in place throughout IMRT, the median maximum movement of the markers during IMRT was 0.59 cm in the right–left direction (range, 0–0.9), 1.46 cm in the anterior–posterior direction (range, 0.8–2.79), and 1.2 cm in the superior–inferior direction (range, 0.6–2.1). Large variations in rectal or bladder volume frequently correlated with significant displacement of the vaginal apex.

Conclusion: Although treatment with a full bladder is usually preferred because of greater sparing of small bowel, our data demonstrate that even with detailed instruction, patients are unable to maintain consistent bladder filling. Variations in organ position during IMRT can result in marked changes in the position of the target volume and the volume of small bowel exposed to high doses of radiation.

Vagina Contouring

- Image registration issues
- Need to generate consistent guidelines



Dilator during RT

Reproducibility and genital sparing with a vaginal dilator used for female anal cancer patients

Tina Marie Briere [a,*], Christopher H. Crane [b], Sam Beddar [a], Priya Bhosale [c], Henry Mok [b], Marc E. Delclos [b], Sunil Krishnan [b], Prajnan Das [b]

[a] Department of Radiation Physics; [b] Department of Radiation Oncology; and [c] Department of Diagnostic Radiology, UT MD Anderson Cancer Center, Houston, TX, USA

Purpose: Acute vulvitis, acute urethritis, and permanent sexual dysfunction are common among patients treated with chemoradiation for squamous cell carcinoma of the anal canal. Avoidance of the genitalia may reduce sexual dysfunction. A vaginal dilator may help delineate and displace the vulva and lower vagina away from the primary tumor. The goal of this study was to evaluate the positional reproducibility and vaginal sparing with the use of a vaginal dilator.

Materials and methods: Ten female patients treated with IMRT for anal cancer were included in this study. A silicone vaginal dilator measuring 29 mm in diameter and 114 mm in length was inserted into the vagina before simulation and each treatment. The reproducibility of dilator placement was investigated with antero-posterior and lateral images acquired daily. Weekly cone beam CT (CBCT) imaging was used to confirm coverage of the GTV, which was typically posterior and inferior to the dilator apex. Finally, a planning study was performed to compare the vaginal doses for these 10 patients to a comparable group of 10 female patients who were treated for anal cancer with IMRT without vaginal dilators.

Results: The absolute values of the location of the dilator apex were 7.0 ± 7.8 mm in the supero-inferior direction, 7.5 ± 5.5 mm in the antero-posterior, and 3.8 ± 3.1 mm in the lateral direction. Coverage of the GTV and CTV was confirmed from CBCT images. The mean dose to the vagina was lower by 5.5 Gy, on average, for the vaginal dilator patients, compared to patients treated without vaginal dilators.

Conclusion: The vaginal dilator tended to be inserted more inferiorly during treatment than during simulation. For these ten patients, this did not compromise tumor coverage. Combined with IMRT treatment planning, use of a vaginal dilator could allow for maximum sparing of female genitalia for patients undergoing radiation therapy for anal cancer.

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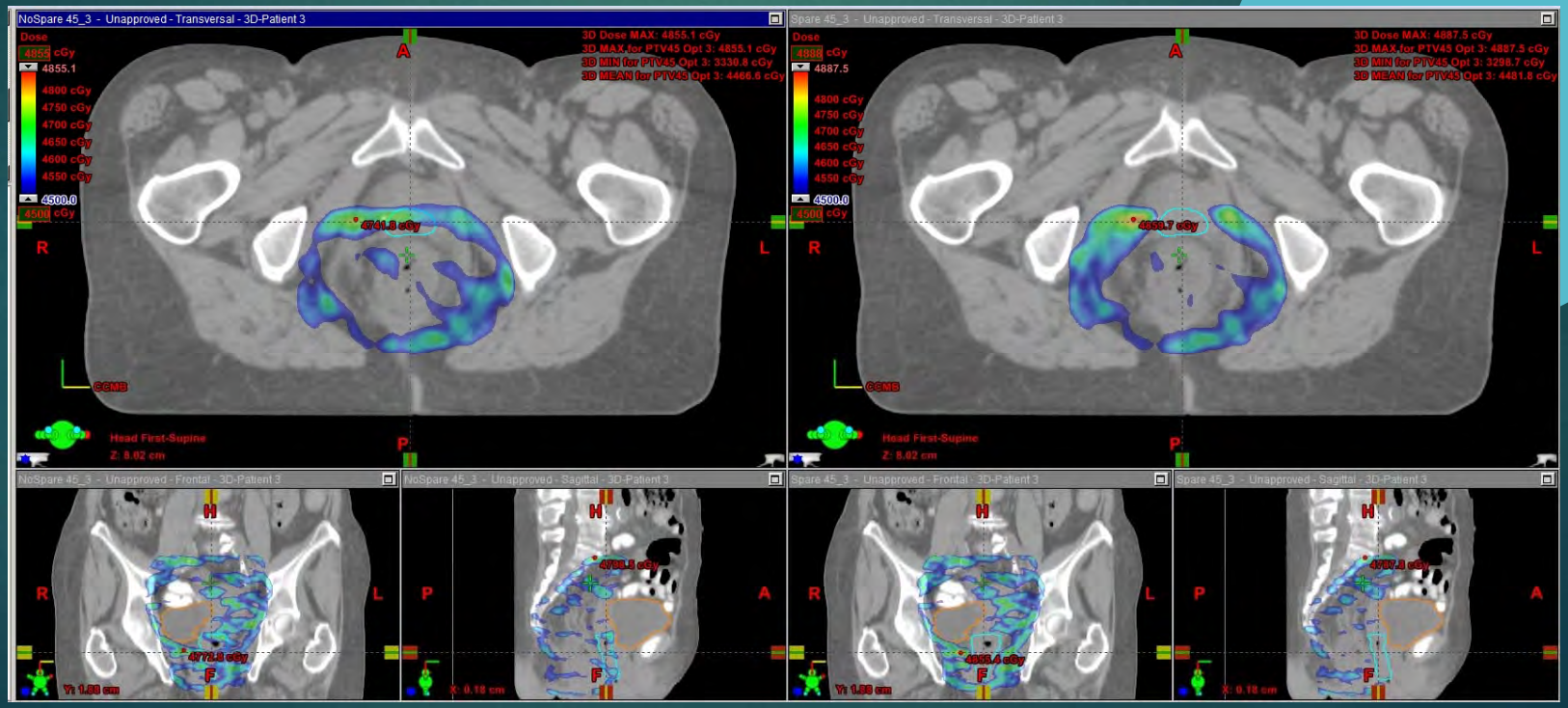
IGRT

- IGRT improvements → Smaller margins → Less vagina in field
- Daily vagina assessment
- Adaptive radiotherapy
- Bladder filling

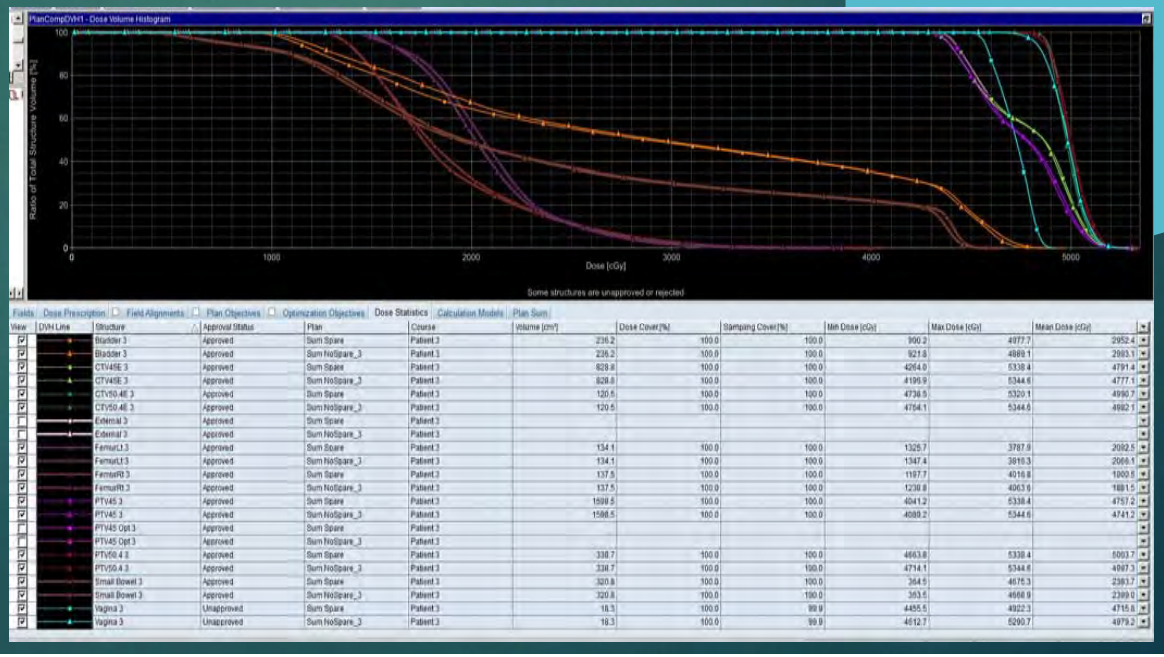
Concerns

- Potential risk of marginal relapse



Conclusion

- VMAT planning using an objective to spare the vagina can significantly reduce the volume of vagina receiving 50Gy, as well as the Dmax and Dmean, without compromising target coverage or adjacent organs at risk dose constraints.



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Thank you!