On Some Contributors to Uncertainties in GYN IGBT

Duke Experience

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- NO FINANCIAL RELATIONSHIPS TO DISCLOSE

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Overview

- Do we need MRI for each fraction?
- Role of vaginal balloon packing systems
- Intelligent dose summation
- Do we need MBDCA for GYN?
- In-vivo dosimetry for treatment delivery verification

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Do we need MRI for each fraction?

- UNCLEAR, if use of MRI beyond the first fraction is useful in clinical practice.
- Or is the HRCTV changing from FX to FX?
- Or it is not changing in reality, but it is contoured differently?
- Duke experience with MR-based planning
  - Variation among fractions
  - Clinical/meaningful differences in dose to target

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J Chino et al., WCB 2012

Methodology

- We retrospectively identified 8 PT (39 FXs)
- CT and MRI for each FX
- Contoured as per the GEC-ESTRO for target delineation (HR CTV, IR CTV) and OAR.
- Planning for each fraction was done in BrachyVision 8.10 (Varian Corp., Palo Alto, CA)
- Subset of 35 HRCTVs retrospectively re-contoured in one sitting (blinded to original HRCTVs)
- The total time from insertion to TX was also recorded.

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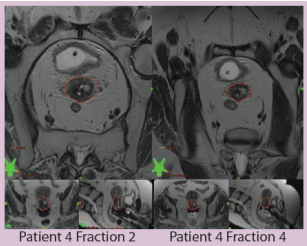
J Chino et al., WCB 2012

Accord Across Fractions



Patient 4 Fraction 2 Patient 4 Fraction 4

Figure 1. MRI based HRCTV contours for patient 4 showing good accord across fractions with minimal volume diffence. Plans varied to optimize sparing of normal tissue on each fraction.

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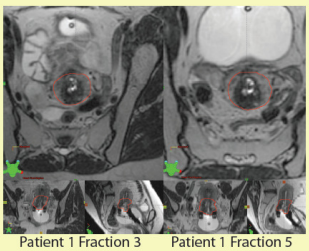
J Chino et al., WCB 2012

Slight Difference Across Fractions



Patient 1 Fraction 3 Patient 1 Fraction 5

Figure 2. MRI based HRCTV contours for patient 1 showing subtle volume diffences due to tandem rotation within the pelvis. Plans varied to optimize sparing of normal tissue on each fraction

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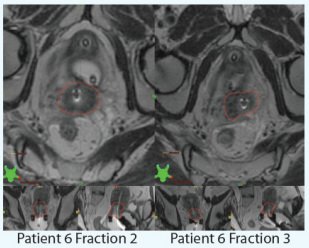
Discord Across Fractions



Patient 6 Fraction 2 Patient 6 Fraction 3

Figure 3. MRI based HRCTV contours for patient 6 showing large deviation of the HRCTV due to tandem divergence into the myometrium during placement. Plans varied to cover HRCTV and spare normal tissues.

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J Chino et al., WCB 2012

HRCTV Volume Variation Between FXs

- Among individual women,
  - range = 37 - 73% of the woman's median value, (10-28 cc absolute difference), median range = 47% (absolute range 11 cc)
- Recontoured HRCTVs:
  - range = 16-76% of the woman's median value, (2-20 cc absolute difference), median range = 33% (absolute range 8 cc)
- HRCTV D90 Median dose = 663cGy,
- HRCTV D90 doses range was 4-13% of the woman's median value (26-86cGy absolute difference).
- The median time of procedure = 3.7 hrs (IQR 3.3 – 4.1 hrs).

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So, do we need MR for each FX?

- Yes, based on our data.
- The HRCTV volumes were variable between fractions, and resulted in variability in the plans developed to meet GEC-ESTRO dose goals.
- This variability was less with retrospective “single sitting” re-contouring but was still up to 76% of the median volume in some women.
- However, MRI based TP also requires significant time and access to resources and resources, which should be factored into the decision to implement for all fractions.

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J Chino et al., WCB 2012

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Role of vaginal balloon packing system

- With such still long treatment procedures there is increased need for very good, controllable, customized packing
- RadiaDyne Alatus Balloon
- Advantages
  - Pushes away normal tissue
  - Compatible with T&R and T&O
  - Fiducials for depth verification
  - Balloon can expand and conform to patient anatomy and applicator
  - Improved dosimetry
- **Balloon role in maintaining implant stability**

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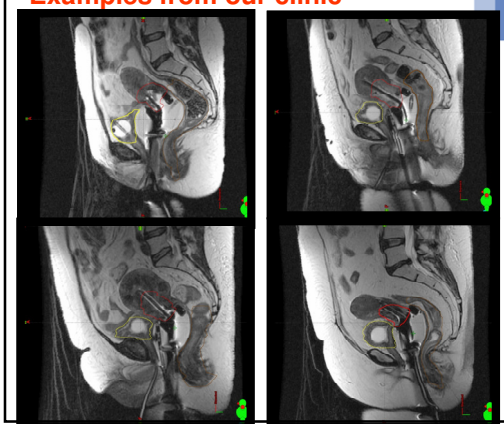
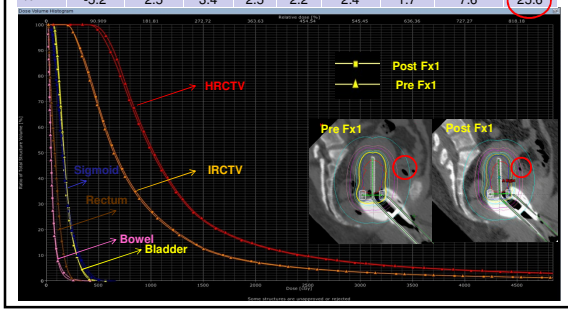
Examples from our clinic



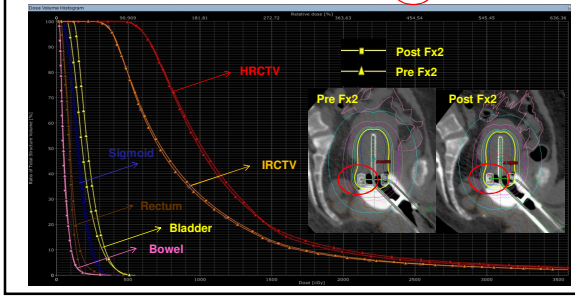
Pre vs. Post Plan, FX1

	HRCTV D90	HRCTV D100	IRCTV D100	A_Lt	A_Rt	Bladder D2cc	Rectum D2cc	Sigmoid D2cc	Bowel D2cc
Pre	640	365	320	593	547	370	230	410	250
Post	607	374	331	608	559	379	234	441	314
%	-5.2	2.5	3.4	2.5	2.2	2.4	1.7	7.6	25.6



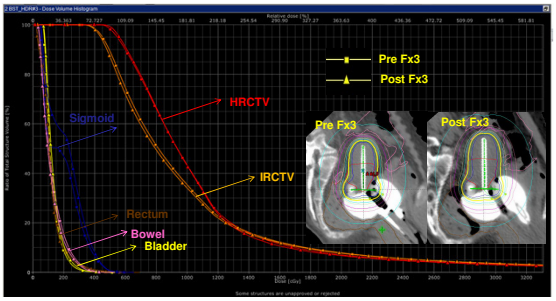
Same Patient, FX2

	HRCTV D90	HRCTV D100	IRCTV D100	A_Lt	A_Rt	Bladder D2cc	Rectum D2cc	Sigmoid D2cc	Bowel D2cc
Pre	663	425	429	586	591	400	230	290	223
Post	669	452	428	597	602	397	164	302	279
%	0.9	6.4	-0.2	1.9	1.9	-0.7	-28.7	4.1	25.1



Different Patient, FX3

	HRCTV D90	HRCTV D100	IRCTV D100	A_Lt	A_Rt	Bladder D2cc	Rectum D2cc	Sigmoid D2cc	Bowel D2cc
Pre	609	445	478	567	552	280	330	429	379
Post	598	426	492	526	601	262	373	413	420
%	-1.8	-4.3	2.9	-7.2	8.9	-6.4	13.0	-3.7	10.8



Role of Packing System: Conclusion

- Large changes (>10 %) observed mostly in bowel and rectum. We isolated the rectum changes in contouring issues, more than change in filling and location.
- Overall, the balloon packing system role can maintain the quality of the implant over the duration of a typical T&R or T&O treatment (3-4 hrs).

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Intelligent Dose Summation: Proof of Concept

- Summation of doses relies currently on point EQD2 dose additions of target and OAR metrics form the EBRT and BT plans.
- To correctly sum doses in 3D we have to account for:
  - Applicator position relative to anatomy, or lack of (in EBRT)
  - OAR deformation (differential filling in most OARs of interest)
  - Account for radiobiologic differences between EBRT and BT
  - Account for dose inhomogeneities in IMRT plans
- Investigate **DEFORMABLE IMAGE REGISTRATION (DIR)**

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Clinical Commercial Software

- VelocityAI (Velocity Medical, Atlanta, GA)
- RTx (Mirada Medical Ltd., Oxford, UK)
- MIM Software™ (Cleveland, OH)
  - Free form intensity-based deformable registration algorithm
  - *Piper JW. Evaluation of An Intensity-Based Free-Form Deformable Registration Algorithm. Medical Physics. June 2007;34(6):2353-2354.*
- Others…??

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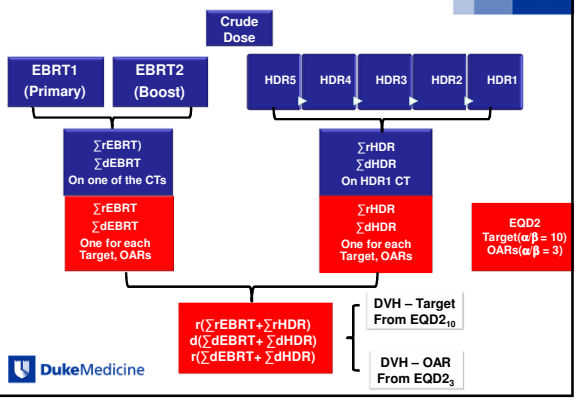
Registration Process



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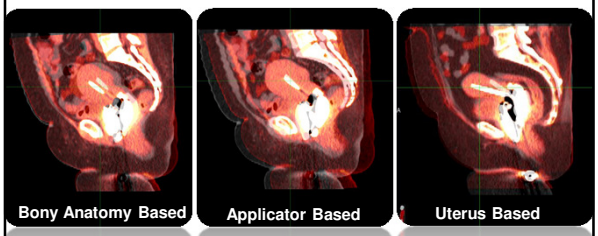
Registration Rules

- EBRT: Rigid registration first, then deformable
- BT (HDR): Rigid first based on applicator if same tandem length/angle, or uterus if different. NOT based on BONE!



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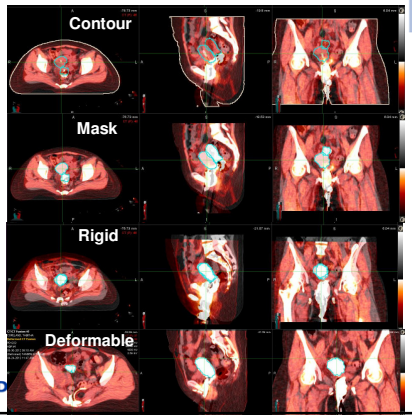
- When applicator/uterus off from FX to FX, mask uterus (HU = 1000)



Duke Clinic Examples

- P1: EBRT + 5 HDR FXs (5 HDR insertions): same applicator
  - EBRT: 45 3D conformal to pelvis and PA nodes
  - HDR: T&R 27.5 Gy in 5.5 Gy/fx
- P2: EBRT + 5 HDR FXs (1 HDR insertion)
  - EBRT: 45 Gy pelvis + integrated boost 55 Gy to nodes + 12.6 Gy sequential boost
  - HDR: T&R 27.5 Gy in 5.5 Gy/fx
- P3: EBRT+ 5 HDR FXs (5 HDR insertions): mix of applicators
  - EBRT: 45 Gy 3D conformal
  - HDR: T&R 27.5 Gy in 5.5 Gy/fx (2 FX T&O and 3 FXs T&R)

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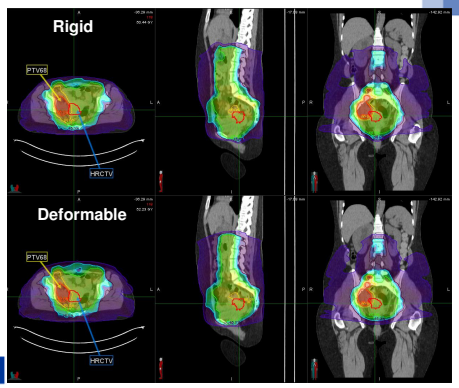
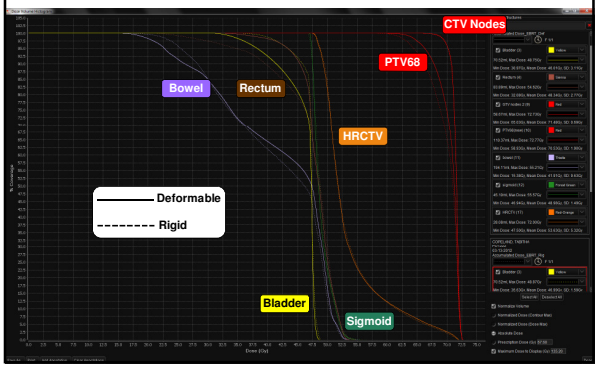
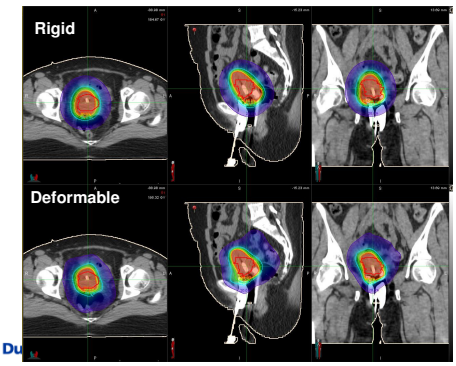
P2->: EBRT Pri + Bst (Rigid vs. Deformable)



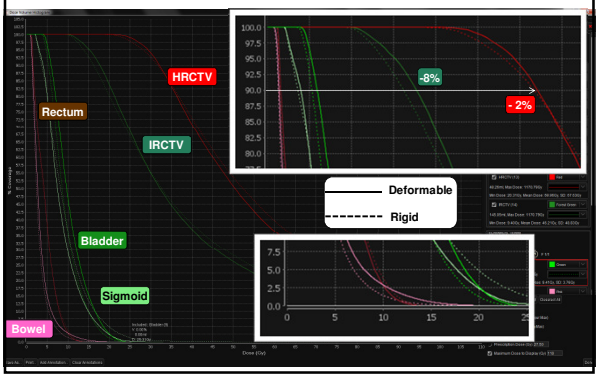
P2->cDVH: EBRT Pri + EBRT Bst Rigid vs. Deformable



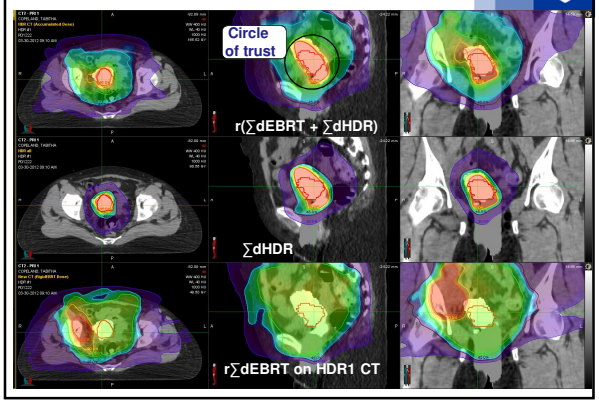
P2->One insertion(5FXs): ∑5 HDR FXs Rigid vs. Deformable on HDR1 CT



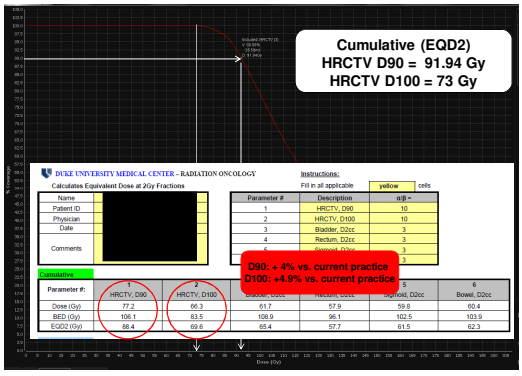
P2->cDVH: One insertion(5FXs) ∑ 5HDR FXs Rigid vs. Deformable on HDR1 CT



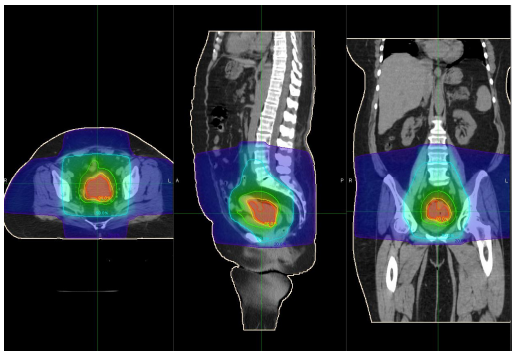
P2->r(∑dEBRT + ∑dHDR) for Target(HRCTV)



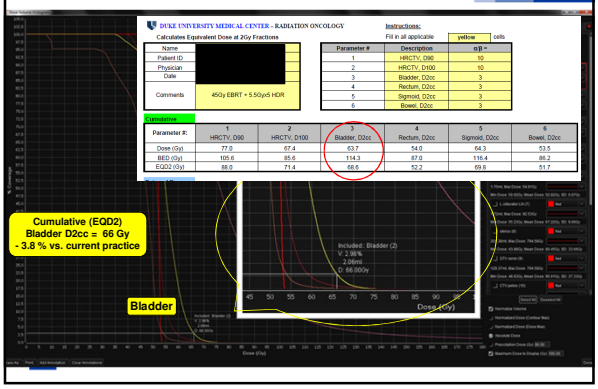
P2/DVH: r(∑dEBRT +∑dHDR) for Target(HRCTV)



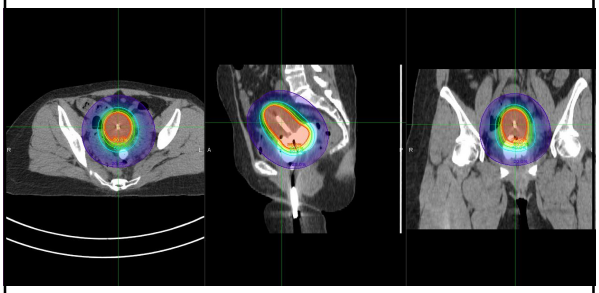
P1-Five insertion(5FXs): EBRT+5 HDR FXs (Deformable on EBRT CT)



P1/DVH: d(∑dEBRT + ∑dHDR) for OARs



P3->Five insertion(5FXs): 2 FX T&O, 3 FX T&R (Deformable on HDR1 CT)



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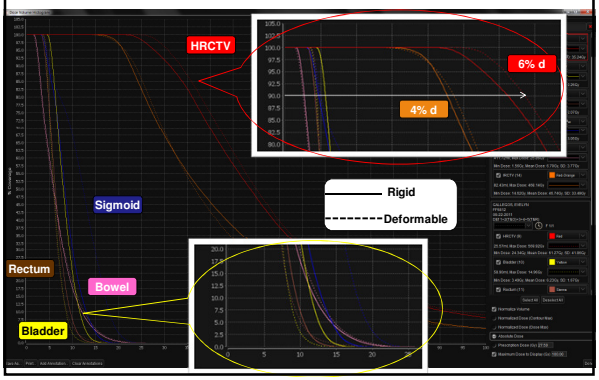
P3->DVH (Crude)-One insertion(2 T&O, 3 T&R) Rigid vs. Deformable



Intelligent Dose Summation

- Posible aid to keep uncertainties in check
- Requires DIR
  - Very challenging for GYN cervix cancer patients due to change in topography between the EBRT and HDR
- We have to understand the limitations of the DIR algorithm used and control each step.
- We have to generate more data to understand patient-dependent variations.

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TG-43 dosimetry formalism

- **Defines water as reference medium**
- Tissue is not water-equivalent
- Variable/dynamic scattering conditions
- Doesn't account for source/applicator shielding

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BV ACUROS® (BrachyVision, Varian): Grid-Based Boltzman Solver (GBBS)

- Alternative to MC with similar accuracy, but increased efficiency
- Deterministic solver of the differential linear Boltzmann transport equation (LBTE)
- Accounts for the effect of applicators (use of solid applicators libraries)
- Accounts for the different tissue types
- Accounts for the effects of the patient boundaries

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Existent studies

- Libby, Ter-Antonyan, Schneider, Brachytherapy , vol 10 (S1, S66), 2011 – abstract, not too many details

Structure	Acuros™	TG43	Difference
ICRU38 Bladder	393 ± 89 cGy	417 ± 91 cGy	5.9 ± 1.1%
ICRU38 Rectum 1	234 ± 57 cGy	259 ± 61 cGy	9.8 ± 1.6%
ICRU38 Rectum 2	273 ± 88 cGy	300 ± 92 cGy	9.3 ± 1.5%
Bladder Mean dose	243 ± 55 cGy	260 ± 55 cGy	6.9 ± 2.9%
Rectum Mean dose	151 ± 30 cGy	161 ± 30 cGy	5.8 ± 1.1%

- Mikell et al, 2012, IJROBP, T&O
  - +/- overriding patient contour to 1 g/cm3 muscle
  - +/- overriding contrast material to muscle or bone
  - majority of metrics < 5%: A, B, D2 cc bladder, ICRU bladder, regardless of the masking of balloon contrast
  - BV-ACUROS-based dose calculations have minimal clinical impact;

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Establish relevance of using BV-ACUROS for HDR Cervical Cancer Patients

- 5 patients (**T&R**)
- 22 fractions
- Clinical plans calculated with TG43 and BV-ACUROS
- HRCTV D90 and D100 [%RX]
- Manchester Point A [%RX]
- Bladder, Rectum, Sigmoid, Bowel D0.1 cc, D2cc, D10cc [Gy]
- Solid Model Applicator

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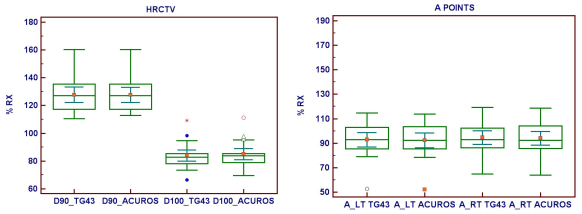
Target: TG43 vs. BV-ACUROS™



Mean % diff < 2%

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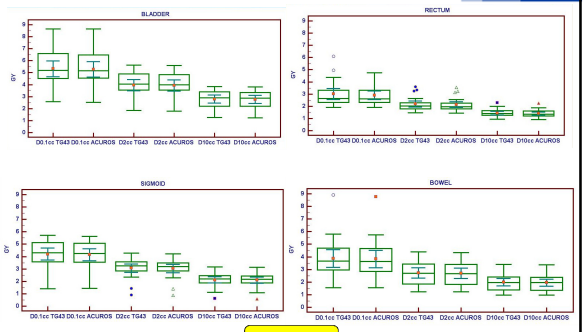
OARs: TG43 vs. BV-ACUROS™



Mean % diff < 2%

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Our Conclusions

- Like MD Anderson Group, Mikell et al, we concluded that BV-ACUROS-based dose calculations have minor clinical impact in GYN cases that use non-shielded applicators.
- Await the recommendations of TG 186 for MBDCA and continue to generate data to include in larger multi-institution comparisons.

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Role and need for in-vivo dosimetry

- With complex and lengthy planning and treatment procedures required by IGBT there is increased need for validation of delivered doses;
- Investigate the use of Presage Dosimetry for HDR procedures:
  - develop system to read small dosimeters;
  - calibrate dosimeters at Ir-192 energy and body temperature;

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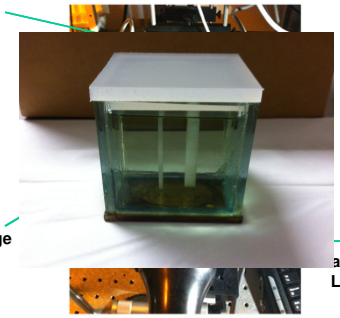
Imaging Set Up



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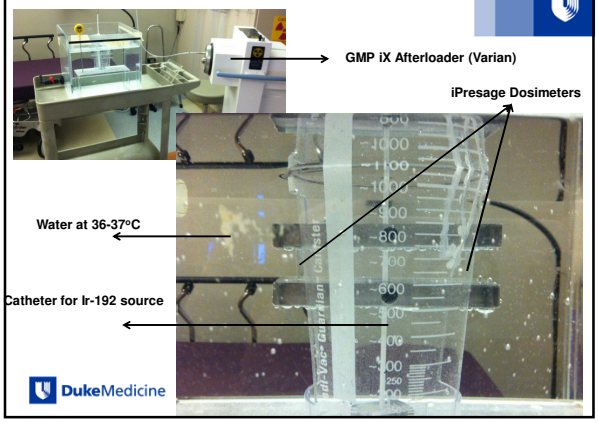
M Oldham's Dosimetry Lab, Duke Univ.

Experiment Set Up for iPD Calibration at Ir-192 Energy



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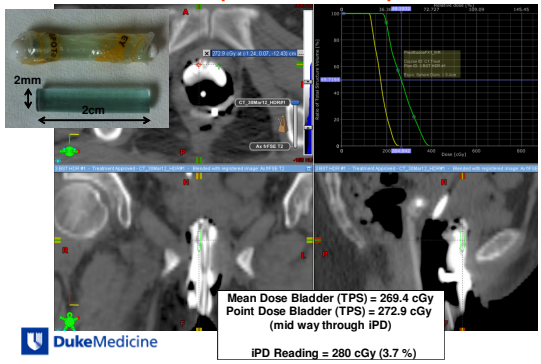
T&R Patient: 1 iPresage Dosimeter on Alatus Balloons (Bladder Side)



Mean Dose Bladder (TPS) = 269.4 cGy
Point Dose Bladder (TPS) = 272.9 cGy
(mid way through iPD)

iPD Reading = 280 cGy (3.7 %)

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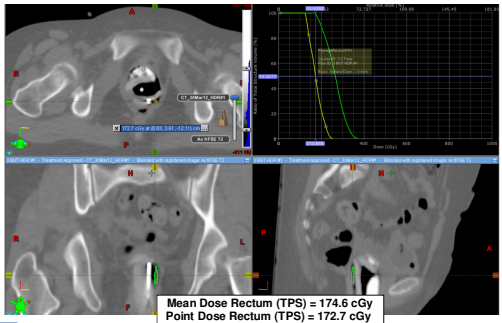
T&R Patient: 1 iPresage Dosimeter on Alatus Balloons (Rectum Side)



Mean Dose Rectum (TPS) = 174.6 cGy
Point Dose Rectum (TPS) = 172.7 cGy
(mid way through iPD)

iPD Reading = 167 cGy (-3.5%)

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Conclusion

- Contouring still the largest contributor to uncertainties
  - Aid the process further with functional imaging
- Applicator stability within the planning time frame
  - Optimize insertion, imaging, planning and treatment flows to reduce the overall time
- For GYN with unshielded applicators, TG43-based calculation introduces only minimal uncertainty when compared to MBDCA (BV-ACUROS)
- Intelligent dose summation very challenging but maybe worth having clear defined protocols to assess impact , if any, on local control and late toxicities
- In-vivo dosimetry: yes, if available

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Acknowledgments

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  - Jing Cai, PhD
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  - Beverly Steffey, MS
- Duke Dosimetry Lab
  - Mark Oldham, PhD
  - Adria Vidovic
  - Titania Juang

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