On Some Contributors to Uncertainties in GYN IGBT

Duke Experience

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• NO FINANCIAL RELATIONSHIPS TO DISCLOSE

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
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

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.

Accord Across Fractions

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

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).

Discord Across Fractions

HRCTV Volume Variation Between FXs
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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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
Examples from our clinic

Pre vs. Post Plan, FX1

<table>
<thead>
<tr>
<th>HRCTV D90</th>
<th>HRCTV D100</th>
<th>IRCTV D90</th>
<th>IRCTV D100</th>
<th>A_Lt</th>
<th>A_Rt</th>
<th>Bladder D2cc</th>
<th>Rectum D2cc</th>
<th>Sigmoid D2cc</th>
<th>Bowel D2cc</th>
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<tbody>
<tr>
<td>Pre</td>
<td>840</td>
<td>365</td>
<td>323</td>
<td>593</td>
<td>547</td>
<td>370</td>
<td>230</td>
<td>310</td>
<td>250</td>
</tr>
<tr>
<td>Post</td>
<td>697</td>
<td>374</td>
<td>331</td>
<td>609</td>
<td>559</td>
<td>379</td>
<td>234</td>
<td>441</td>
<td>314</td>
</tr>
<tr>
<td>%</td>
<td>6.2</td>
<td>2.5</td>
<td>3.4</td>
<td>2.5</td>
<td>2.2</td>
<td>2.4</td>
<td>1.7</td>
<td>7.6</td>
<td>26.4</td>
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</table>

Same Patient, FX2

<table>
<thead>
<tr>
<th>HRCTV D90</th>
<th>HRCTV D100</th>
<th>IRCTV D90</th>
<th>IRCTV D100</th>
<th>A_Lt</th>
<th>A_Rt</th>
<th>Bladder D2cc</th>
<th>Rectum D2cc</th>
<th>Sigmoid D2cc</th>
<th>Bowel D2cc</th>
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</thead>
<tbody>
<tr>
<td>Pre</td>
<td>663</td>
<td>435</td>
<td>429</td>
<td>586</td>
<td>591</td>
<td>406</td>
<td>230</td>
<td>290</td>
<td>223</td>
</tr>
<tr>
<td>Post</td>
<td>669</td>
<td>452</td>
<td>428</td>
<td>597</td>
<td>602</td>
<td>397</td>
<td>164</td>
<td>302</td>
<td>279</td>
</tr>
<tr>
<td>%</td>
<td>0.9</td>
<td>6.4</td>
<td>-0.2</td>
<td>1.9</td>
<td>1.9</td>
<td>-0.7</td>
<td>26.7</td>
<td>4.1</td>
<td>25.1</td>
</tr>
</tbody>
</table>
Different Patient, FX3

<table>
<thead>
<tr>
<th></th>
<th>HRCTV DOS</th>
<th>HRCTV D90</th>
<th>HRCTV D100</th>
<th>HRCTV A_Lt</th>
<th>HRCTV A_Rt</th>
<th>Bladder Dose</th>
<th>Rectum Dose</th>
<th>Sigmoid Dose</th>
<th>Bowel Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>609</td>
<td>445</td>
<td>478</td>
<td>567</td>
<td>552</td>
<td>280</td>
<td>330</td>
<td>429</td>
<td>379</td>
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<tr>
<td>Post</td>
<td>598</td>
<td>426</td>
<td>492</td>
<td>526</td>
<td>601</td>
<td>262</td>
<td>373</td>
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</tr>
<tr>
<td>%</td>
<td>-1.8</td>
<td>-4.3</td>
<td>2.9</td>
<td>-7.2</td>
<td>6.4</td>
<td>13.0</td>
<td>-3.7</td>
<td>10.8</td>
<td></td>
</tr>
</tbody>
</table>

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 from 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)

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
- Others…??

Registration Process
**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!

**Applicator Based**

**Uterus Based**

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

Rigid vs. Deformable

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

P2->: One insertion(5FXs): $\sum 5$ HDR FXs
Rigid vs. Deformable on HDR1 CT
P2->cDVH: One insertion(5FXs) Σ 5HDR FXs
Rigid vs. Deformable on HDR1 CT

P2->r(ΣdEBRT + ΣdHDR) for Target(HRCTV)

P2/DVH: r(ΣdEBRT + ΣdHDR) for Target(HRCTV)
P1-Five insertion(5FXs): EBRT+5 HDR Fxs (Deformable on EBRT CT)

P1/DVH: d(∑dEBRT + ∑dHDR) for OARs

Cumulative (EQD2)

Bladder D2cc = 66 Gy - 3.8% vs. current practice

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

- Possible 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

BV ACUROS® (BrachyVision, Varian): Grid-Based Boltzmann 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

Existente studies

- Libby, Ter-Antonyan, Schneider, Brachytherapy, vol 10 (S1, S66), 2011 — abstract, not too many details
  - GEC/ESTRO Dataset 1
  - GEC/ESTRO Dataset 2
  - Multi-dose fraction
  - Printed Silver source

- Mikell et al, 2012, IROBP, 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
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

Target: TG43 vs. BV-ACUROS™

Mean % diff < 2%

OARs: TG43 vs. BV-ACUROS™

Mean % diff < 2%
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;
Imaging Set Up

LED Light Source
Presage Jig
Camera Lens

Experiment Set Up for IPD Calibration at Ir-192 Energy

GMP IX Afterloader (Varian)
Presage Dosimeters
Water at 36-37°C
Catheter for Ir-192 source

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

Mean Dose Bladder (TPS) = 283.9 cGy
Point Dose Bladder (TPS) = 272.0 cGy
(mid way through IPD)
IPD Reading = 280 cGy (3.7%)
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%)

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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