MRI Guided GYN Brachytherapy: Clinical Considerations

AAPM
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Disclosures

• none
Learning Objectives

• Historical Context: Film based Brachytherapy
• Advantages of modern imaging for cervical cancer (CT, MRI)
• GEC-ESTRO recommendations for contouring on MRI
• Clinical results with image guided brachytherapy (IGBT)
• Logistics and challenges of implementing IGBT at our institution
Intracavitary Brachytherapy: Cervical Cancer

• A solution to the problem of giving high dose to a highly mobile tumor in close proximity to bladder and rectum

• 3D conformal, IMRT and SBRT boosts are severely limited by intrafraction and interfraction movement

• Film based treatment has resulted local control rates of ~80%, with grade 3-4 late toxicity of ~15% (RTOG 9001)
LDR T&O set
LDR planning
LDR planning

50-60cGY/hr. For 40Gy (85Gy with 45Gy WPRT) = 72-80hours
Brachytherapy Doses

LDR

• Total doses should be summed with Prior External Beam
• Point A doses should be 75-90 Gy
• Point B doses should be 55-60 Gy
  — May boost sidewall with external beam for IIB disease to an additional 5-15 Gy
• Bladder point should be limited to 75Gy
• Rectal points should be limited to 70Gy
Modern Imaging for Cervical Cancer: Part 1 CT
CT compatible applicators

Conventional LDR FSD applicator

Weeks CT compatible Applicator
CT-Based Planning (OAR)

• Weeks & Montana, developed CT compatible T&O set in 1997 at Duke
  – Systematic underestimation of max bladder and rectal doses with Film based plans

• MD Anderson series from 2005
  – rectal point a reasonable surrogate for rectal max
  – bladder point resulted in systematic underestimation of bladder max

Film Points vs 3D Max Dose

Rectum

Bladder

CT based Planning (Target)

• Michigan Series (Schoeppel, IJROBP 1994)
  – Film Based plans systematically underdose the CT-visible cervix

• Loyola Series (Gao, Brachytherapy 2010)
  – CT defined volume varied greatly between patients (12ml – 39ml)
  – With Film based plans, the cervical dose was 40% lower than prescription in those with high volumes.
Point A isodose

Minimum CTV dose relative to point A:
- 36%
- 49%
- 96%
- 103%
- 134%

CTV’s assessed from MRI
5 pt’s
CT-Based Planning: Limitations

- CT is not to be ideal at determining extent of disease
- Preoperative CT studies show:
  - 50-65% accurate for extent within cervix
  - 75-80% accurate for determining extension outside of cervix

Kim et al. J Comput Assist Tomogr 1993
Subak et al OB GYN 1995
Modern Imaging for Cervical Cancer: Part 2 MRI
T2 weighted MRI as a Imaging Standard

• MRI superior in same preoperative studies compared to CT
  – 75-90% accurate for extent within cervix
  – 85-95% accurate for extension beyond cervix

• Viswanathan (IJROBP 2007) compared CT contours to MRI
  – Found systematic overestimation of cervix with CT
    • 20% median deviation between CT and MRI
    • CT overestimates in the lateral dimension
CT vs MRI
CT vs MRI
GEC-ESTRO recommendations for MRI contouring

- **GTV:** all MRI visible tumor at time of brachytherapy
- **HRCTV:** GTV + cervix + “grey zones” of indeterminate signal (usually in parametrium)
- **IRCTV:** HRCTV + 10mm margin, restricted to 5mm anterior and posterior + initial extent of disease
- Normal tissue including bladder, rectum, sigmoid

Haie-Meder et al. Rad Onc 2005
Potter et al. Rad Onc 2006
Clinical Results: Vienna Group

- 141 women with IB-IVA cervical cancer treated with 45-50.4 Gy, concurrent cisplatin
- First 3 years, dose to HRCTV/IRCTV recorded but not used for optimization
- Last 3 years, dose optimized to cover HRCTV/IRCTV

Dimopoulos et al. IJROBP 2009
Dimopoulos et al. Rad Onc 2009
Clinical Results: Vienna

• HRCTV D90
  – <87Gy resulted in local control of 80%
  – >87Gy resulted in local control of 96%

• HRCTV D100 (D98)
  – <66Gy resulted in local control of 83%
  – >66Gy resulted in local control of 93%

• IRCTV dose was not significantly associated with clinical outcome
Large tumors

Large, non-responding tumors

D90 HR CTV [Gy]

Local control [%]

<60, 60 - <80, 80 - <100, 100 - <120, >120

All Patients

total population
tumour group 2
tumour group 2b

Potter, et al Rad Onc 2009
Toxicity: Vienna

• Same group demonstrated association with late toxicity
• Rectum Grade 2-4 late toxicity:
  – $D_{2cc} 67\text{GY} = 5\%$
  – $D_{2cc} 78\text{Gy} = 10\%$
  – $D_{2cc} 90\text{Gy} = 20\%$
• Bladder Grade 2-4 late toxicity
  – $D_{2cc} 70\text{Gy} = 5\%$
  – $D_{2cc} 101\text{Gy} = 10\%$
  – $D_{2cc} 134\text{Gy} = 20\%$
• No small bowel or sigmoid association noted
<table>
<thead>
<tr>
<th>Volume</th>
<th>2D point analogue</th>
<th>3D dosimetric measures</th>
<th>Dosimetric Goal/Limit</th>
<th>Endpoint</th>
<th>Level of Evidence for Goal/Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRCTV (tumor + cervix + parametrial extent at time of implant)</td>
<td>Point A (2cm superior to ovoids, 2cm lateral to tandem)</td>
<td>D90 D100</td>
<td>D90 &gt; 75-85 Gy D100 &gt; 65 Gy</td>
<td>Pelvic Control &gt;90%</td>
<td>Strong</td>
</tr>
<tr>
<td>IRCTV (HRCTV + margin, + initial extent of disease)</td>
<td>Closest analogue is Point B (3 cm lateral to point A) for IIB disease</td>
<td>D90</td>
<td>D90 &gt; 60-75 Gy</td>
<td>Pelvic Control (no firm data)</td>
<td>Weak</td>
</tr>
<tr>
<td>Bladder</td>
<td>Bladder point (most dependent point of foley balloon)</td>
<td>D2cc</td>
<td>D2cc &lt;90 Gy</td>
<td>G2-4 late toxicity &lt;5-10%</td>
<td>Strong</td>
</tr>
<tr>
<td>Rectum</td>
<td>Rectal point (5 mm posterior to vaginal packing)</td>
<td>D2cc</td>
<td>D2cc &lt;75 Gy</td>
<td>G2-4 late toxicity &lt;5-10%</td>
<td>Strong</td>
</tr>
<tr>
<td>Sigmoid</td>
<td>None</td>
<td>D2cc</td>
<td>D2cc &lt;75 Gy</td>
<td>No firm data</td>
<td>Weak</td>
</tr>
<tr>
<td>Small Bowel</td>
<td>None</td>
<td>D2cc</td>
<td>D2cc &lt;65 Gy</td>
<td>No firm data</td>
<td>Weak</td>
</tr>
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STIC trial: Film vs 3D

- 801 women (705 evaluable) treated with either film based or IGBT (mostly CT)
- Prospective but non-randomized
- Local control @ 2 years
  - 73.9% Film Based
  - 78.5% IGBT (p=0.003)
- Grade 3-4 toxicity
  - 22.7% Film based
  - 2.6% IGBT (p=0.002)

Charra-Brunaud et al. Rad Onc 2012
A European study on MRI-guided brachytherapy in locally advanced cervical cancer

EMBRACE

(ENDORSED BY GEC ESTRO)
EMBRACE: How often can HRCTV and OAR constraints be met?

• 134 cases were reviewed and non-optimized plans were generated (equal time in all activated dwell positions)

• Comparison was made between tandem only vs tandem and vaginal loading (non-optimized)

Nkiwane, Brachytherapy 2013
How good are non-optimized plans?

<table>
<thead>
<tr>
<th></th>
<th>Percent of plans meeting HRCTV constraint</th>
<th>Percent of plans exceeding OAR tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HRCTV D90 IB1</td>
<td>HRCTV D90 IB2</td>
</tr>
<tr>
<td>Tandem only</td>
<td>88%</td>
<td>67%</td>
</tr>
<tr>
<td>Tandem + ring or ovoids</td>
<td>88%</td>
<td>75%</td>
</tr>
</tbody>
</table>

Therefore: small tumors are often adequately treated by uniform loading – more extensive disease may need additional measures (optimization / paracervical needles)
Vienna Applicator

Krisitis et al. IJROBP 2006
Vienna Applicator

Krisitis et al. IJROBP 2006
Vienna Applicator

Krisitis et al. IJROBP 2006
Applicator Selection

• T&R will cover most small tumors
  – Posterior and anteriorly based tumors may benefit from loading the anterior and posterior ring
• T&O: lateral coverage for larger cervical disease
• Vienna: parametrial disease
• Tandem Cylinder/Miami: thin vaginal disease
• Syed template + Tandem: thick vaginal disease
Conclusions from published data

• MRI is superior to CT and film based delineation of tumor
• Doses to MRI based volumes are associated with clinically relevant outcomes
• Doses to the contoured Bladder and Rectum are associated with late toxicity
• IGBT as a technique is associated with decreased toxicity with the same or improved control
Emerging modalities

• DCE-MRI: may reveal areas of poor perfusion, which may be high risk regions
• DW-MRI: may reveal areas of high cellular density (restricted diffusion) which may be high risk areas
• PET-CT: prognostic utility is well established, but uncertain for utility with IGBT
• US: used clinically for decades, but uncertain as of yet how best to integrate this highly accessible modality in the frame work of IGBT
Questions

• Is it exportable?
• Are the metrics currently reported the best?
• Is the method of dose optimization relevant?
• Are there other organs/volumes that should be contoured?
• What are the logistical challenges to making the switch from FBBT to IGBT?
Our Experience

- Film Based through 2005 (LDR)
- CT based IGBT was used throughout 2006-2010 (LDR)
- 2011-present MRI based IGBT used (HDR)
2005

- T&O placed in OR
- Orthogonal Films taken
- Points chosen (A, B, rectum, and bladder)
- Plan devised
- Patient loaded on floor
- 70-80 hours in hospital immobilized
- Implant unloaded, T&O removed
2013

- Patient brought to clinic
- Anesthesia induced (level similar to that used during colonoscopy)
- Applicator selected and placed
- CT immediately obtained (r/o perforation)
- MRI obtained
- CT/MRI fused
- Physician contours fused images (HRCTV on MRI, OAR on CT with MRI assist)
- Treatment plan created
- QA performed
- Treatment delivered
- Applicator removed
- Discharge from clinic

x5
Physical Layout
Team Members

• Radiation Oncology (1 attending, 1 resident)
• Anesthesiologist (1 attending +/- 1 CRNA)
• Physics (2 faculty, 1 resident)
• CT/MR operators (3+ therapists/techs)
• Nursing (1 RN + support at recovery)
• It is critical that this be a stable team, for both patient safety, and for efficient use of time
Average Case

- 7:30 am Patient arrives – obtain IV access, premeds (RN)
- 8:00 am Patient to suite, anesthesia induced (MD)
- 8:15 am Applicator selected and placed (MD)
- 8:30 am Anesthesia recovery (RN)
- 8:45 am CT scan (Tech)
- 9:15 am MRI scan (Tech)
- 10:00 am MRI/CT fused (Physics)
- 10:30 am Physician contours (MD)
- 11:00 am Plan optimized (Physics/MD)
- 11:15 am Plan approved (MD)
- 11:30 am Plan/Afterloader QA (Physics)
- 12:00 pm Patient treated (MD/Physics)
- 12:15 pm Applicator Removed (MD)
- 1:00 pm Patient discharged (RN)
The median time from start of imaging to treatment delivery was 3.6 hours (3.3 – 3.9 hours ).
Why plan each time?

• Eliminating the MRI on subsequent fractions would improve throughput and lessen burden on team
Intrafraction Variations

- Applicator change
- HRCTV/IRCTV variations
- OARs variations
Changes in HRCTV contours

Blue box = range of HRCTV volumes as contoured at time of treatment

Green box = range of HRCTV volumes when recontoured in single sitting (retrospective)

There remains a significant variation in contouring, which is reduced but not eliminated by a more consistent approach.
Patient with Good Accord
Patient with Minor Variation

Patient 1 Fraction 3

Patient 1 Fraction 5

DukeRadOnc
Patient with Large Variation

Patient 6 Fraction 2

Patient 6 Fraction 3
Pitfalls/Cautions

- Team needs excellent and open communication
- Schedule needs tight coordination
- MDs and Physics need to perform their work safely and efficiently
- Image fusion and applicator reconstruction need to be done with care
- Dose optimization should be approached stepwise from a more standard film based plan
- Particular attention should be paid to QA prior to treatment by all members of team
The Duke Brachytherapy Team

- Oana Craciunescu PhD
- Jing Cai PhD
- Beverley Steffey MS
- Sheridan Meltsner PhD
- Kimberley Maingat RN
- Danielle Raya RN
- + many more therapists, rad techs, and support staff