Use of MR for Brachytherapy Target Definition and Planning--Cervix Cancer

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• No disclosures
ABS Consensus Guidelines

“Where do we go for guidance?”

• 2012 Viswanathan et al:
  • Locally advanced cervix cancer
• Advances in 3D imaging
  – 3D tissue contouring guidelines
  – New dosimetry nomenclature
  – Improved outcomes (initial reports)
• For implementation
  – 3D contouring
  – image-based treatment planning
  – dose reporting
• ABS Consensus Guidelines recommend adoption of the GEC-ESTRO recommendations

GEC-ESTRO Recommendations

• 2005 Haie-Meder et al
  – 3D-image-based approach and terminology for GTVs and CTVs
  – Based on the clinical experience of 3 different institutions
• 2006 Potter et al
  – 3D dose-volume parameters (D0.1cc, D2cc, EQD2 sums)
• 2010 Hellebust et al
  – Applicator reconstruction in 3D images (CT vs MR)
• 2012 Dimopoulos et al
  – MR imaging principles & technique

Clinical Implementation ca 2007

- First assessment of use of 3D-image based brachy (in mostly the U.S.) in 2007
- 133 ABS physician members surveyed
- 119 members were from U.S.
- Distribution of **imaging modalities** used specifically for dose specification

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<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>All members (n = 133)</th>
<th>U.S. members only (n = 119)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plain film</td>
<td>43% (57)</td>
<td>43% (51)</td>
</tr>
<tr>
<td>CT</td>
<td>55% (73)</td>
<td>56% (67)</td>
</tr>
<tr>
<td>MRI</td>
<td>2% (3)</td>
<td>&lt;1% (1)</td>
</tr>
</tbody>
</table>

Clinical Implementation ca 2007

- How were they **specifying** dose on these images?

<table>
<thead>
<tr>
<th>Prescription, target</th>
<th>All members (n=133)</th>
<th>U.S. members only (n=119)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Point A</td>
<td>76% (101)</td>
<td>77% (92)</td>
</tr>
<tr>
<td>mg/h/Point A</td>
<td>3% (4)</td>
<td>3% (3)</td>
</tr>
<tr>
<td>Volumetric</td>
<td>14% (19)</td>
<td>13% (15)</td>
</tr>
<tr>
<td>Point A and</td>
<td>7% (9)</td>
<td>8% (9)</td>
</tr>
<tr>
<td>volumetric</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prescription, OAR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICRU</td>
<td>52% (69)</td>
<td>54% (64)</td>
</tr>
<tr>
<td>DVH</td>
<td>19% (25)</td>
<td>16% (19)</td>
</tr>
<tr>
<td>Both</td>
<td>29% (39)</td>
<td>30% (36)</td>
</tr>
</tbody>
</table>

- How were they **modifying** dose?
  - More common to modify based on OARs: ICRU points vs DVHs
  - “Very disparate” criteria for target dosing: Point A vs CTV or GTV and what dose?
How to image with MRI?
How to plan with MRI?
GEC-ESTRO/clinical experience
Learning Objectives

• To learn about one example of an implementation of an MRI-based technique for cervix cancer brachytherapy (at WUSM)

• To learn about aspects of this technique in the context of published recommendations and literature

• → To gain an understanding of how MRI can be used for target definition and adaptive treatment planning
Overview of Technique at WUSM

- Dose Prescription
- Implant
- MRI Acquisition
- Treatment Planning
- Dosimetry: Tracking & Adaptation
Dose Prescription

- Tumor stage & size
- IMRT
  - PTV (pelvic and para-aortic lymph node bed) 50.40 Gy at 1.8 Gy fraction, 28 fx
  - MTV Cervix (FDG-PET) 20.0 Gy concurrent
- HDR Brachy in 6 fx
- Timing (Concurrent):
  - IMRT 4 fx per week
  - Brachy 1 fx per week
  - 53 days (Fyles et al.) or else tumor control dropped by 1% per day

J. Esthappan et al., IJROBP 2008; 72,1134-1139.
Kidd et al., IJROBP 2010; 77(4):1085-1091.
Implant

- Semi-sterile
- In HDR suite
- Titanium tandem and ovoids
- Packing
  - Dry gauze, saline-soaked gauze, commercially available balloons
GEC ESTRO: T2W-MRI

- T2W – “golden standard” for visualization of tumor and OARs
- Complementary MRI sequences – optional

WUSM: Multi-sequence MRI

• 1.5-T MRI, 4-channel pelvic coil, respiratory triggering
  – T2-weighted (T2W) turbo spin-echo (TSE) imaging
  – Single-shot diffusion-weighted (DW) echo-planar imaging
  – Proton-density weighted (PDW) TSE imaging
• Para-sagittal acquisitions
• 3-6 minutes per sequence
• Image datasets exported to TPS
• Images registered based on DICOM coordinates (checked to see if patient moved between scans)
T2W: Primary Dataset for Planning

• WUSM & GEC-ESTRO
  – T2W-MRI is the primary dataset for planning
  – Points (e.g., point A)
  – OARs (bladder, rectum, and sigmoid)

• Target volume
  – GEC-ESTRO: GTV as well as HR-CTV defined on T2W-MRI (JKS’s talk)
  – WUSM: GTV defined using T2W and **Diffusion-weighted MRI** sequences
Diffusion-weighted MRI

- DW-MRI
  - Add diffusion-weighted gradients to T2W $\rightarrow$ DWI $\rightarrow$ sensitive to the motion of water molecules
  - Water diffusion properties of different tissues can be quantified on the DWI as an Apparent Diffusion Coefficient (ADC) value

$$S_{DW} = S_o e^{-b*ADC}$$

- $S_{DW}$ and $S_o$ are signal intensities measured with and without diffusion-weighted gradients, respectively
- $b$-value is the diffusion factor (sec/mm$^2$) -- characterizes strength of the diffusion gradients

$\rightarrow$DW-ADC maps
Diffusion-weighted ADC Maps

- DW-ADC maps
  - Cervix tumors have been shown to have significantly lower ADC values than normal cervix
  - More cellularly dense → restricts diffusion → lower ADC value → appears darker
  - WUSM: DW-ADC maps fused with T2W images for the delineation of GTV
  - → Examples

Harry et al., Gynecol Oncol;116:253-261
A para-sagittal slice in the T2W-MRI (a) and corresponding ADC map (b) about 1.5 cm lateral to the tandem for Patient 1. GTV$_B$ defined using both datasets – good agreement between the contour and the image.

Fair agreement—but use with caution!!!

Same patient, same scan, different slice, which contains the tandem. Pitfall: DWI highly sensitive to metal susceptibility artifacts. ADC map and T2W should be used together for GTV_B definition, but the ADC used with caution when near metal.
WUSM: Target Volume Definition

- 2013 Olsen et al: Pretty good agreement between FDG-PET (bright) and DW-ADC maps (dark)

- 2014 Dyk et al: GTV only--dose to GTV from our treatment approach is highly correlated with local control


Applicator Reconstruction

GEC-ESTRO and published literature…

• GE: Centers used T2W-MRI and plastic applicators
• GE: Mentions differences between Plastic vs Titanium applicators:
  – More info: 2009 Haack et al
  • Plastic: weak signal on T2W, use of markers
  • Titanium: susceptibility artifact, can introduce more distortions

Applicator Reconstruction

- GE: Centers used “low” (0.1-0.5 T) and “high” (1.0-1.5-T)
- GE: Mention Ti artifacts and increase at higher Tesla
  - More info: 2011 Kim et al
  - 3-T MRI units offers higher SNR
    - Artifacts increase with higher magnetic strength
    - Worse on T2W (6.9 ± 3.4 mm) vs. T1W (2.6 ± 1.3 mm)
- GE: Phantom MRI scans of Ti using clinical sequences fused against CT

- GE: Alternative planning strategy for Ti: CT or additional MRI sequences fused to the T2W-MRI

Proton Density-Weighted MRI

- WUSM: PDW sequence fused to the T2W-MRI for applicator reconstruction
- TE for PDW << TE for T2W sequence
- Data is acquired at this very short time point
- Signal from tissues in PDW sequence is higher than T2W sequence

Courtesy of Y. Hu
• Tissues brighter in PDW
• Applicator appears dark in both sequences
• → Higher contrast between applicator and tissues in PDW images
• Better visualization of applicator in the PDW images
• Less distorted in PDW images
WUSM: Applicator Reconstruction

- Higher signal in PDW → thinner slices
- 5 mm vs 2.5 mm
- Better visualization of applicator in reconstructed views in PDW
- “Lose” tandem in T2W

Hu and Esthappan et al, *Radiation Oncology* 2013: 8:16
Dosimetry (GEC-ESTRO & Vienna Group)

- 2006 GEC-ESTRO
  - Dose-volume metrics: D2cc – dose to maximally exposed 2 cm³ of the OARs, D90 GTV and HR-CTV
  - “Equivalent dose” and summation: EQD₂: physical \( \rightarrow \) BED \( \rightarrow \) normalized to equivalent dose delivered in 2 Gy fractions of EB
  - Adapting dose to improve target coverage
- 2007 Lang et al
  - Summation spreadsheets with full EB dose, dose constraints
- 2005 Kirisits et al
  - Dose constraints & dose adaptation schemes
  - Start with standard loading, then 4 options:
    - Symmetric scaling via point A
    - asymmetric \( (A_L \text{ vs } A_R) \)
    - changing of dwell positions (ring)
    - changing dwell weights individually

WUSM: Dose Tracking

- Export of DICOM RT files to an in-house developed tool → a tracking spreadsheet (Baozhou et al IJROBP 2014;90(1):S490).
- BT dose tracked per fraction (D2cc bladder)
- Ratios to Point A (e.g., D2cc B < 80%)
- Mean brachy doses projected out to end of treatment and summed with mean IMRT dose
- Kirisits: D2cc B< 90 Gy\(_{\alpha\beta3}\), D2cc R & S<75 Gy\(_{\alpha\beta3}\), D90 GTV >=80-85 Gy\(_{\alpha\beta10}\)
WUSM: Dose Adaptation

• Start with standard loading schemes normalized to point A

• (1) Applicator Optimization:
  – Customize dose by modifying the applicator geometry based on tumor/anatomy
    • e.g., use of mini-ovoids or tandem alone for the latter fractions
  – Can also be used to decrease OAR dose predicted by Dose Tracker

• (2) Loading Optimization:
  – Another way to decrease OAR dose predicted by Dose Tracker
  – Tumor dosing takes priority, loading rules followed for the first 3 fx, regardless of OAR dose
  – After fraction 3, given adequate tumor volume shrinkage (50%), if D2cc out of tolerance…
    ∙ Scale down loading uniformly by either 10% or 20%, while maintaining target coverage
Exp: Dose Tracking & App Optimization

Fx 1 – 3:
Rx isodose colorwash
GTV in red
High bladder doses
Mini ovoids by Fx3

Courtesy of C. Bertelsman

<table>
<thead>
<tr>
<th>OAR-Bladder</th>
<th>BTFX1</th>
<th>BTFX2</th>
<th>BTFX3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vol (cc)</td>
<td>51.21</td>
<td>41.86</td>
<td>44.34</td>
</tr>
<tr>
<td>D100 (Gy)</td>
<td>1.29</td>
<td>1.30</td>
<td>1.18</td>
</tr>
<tr>
<td>D90 (Gy)</td>
<td>1.88</td>
<td>1.91</td>
<td>1.73</td>
</tr>
<tr>
<td>D Mean (Gy)</td>
<td>3.40</td>
<td>3.62</td>
<td>3.20</td>
</tr>
<tr>
<td>D Max (Gy)</td>
<td>6.81</td>
<td>6.75</td>
<td>6.92</td>
</tr>
<tr>
<td>D2cc (Gy)</td>
<td>0.02</td>
<td>0.99</td>
<td>0.76</td>
</tr>
<tr>
<td>EQD2 (Gy), D100</td>
<td>1.10</td>
<td>1.12</td>
<td>0.98</td>
</tr>
<tr>
<td>EQD2 (Gy), D90</td>
<td>1.83</td>
<td>1.87</td>
<td>1.63</td>
</tr>
<tr>
<td>EQD2 (Gy), D Mean</td>
<td>4.35</td>
<td>4.78</td>
<td>3.95</td>
</tr>
<tr>
<td>EQD2 (Gy), D Max</td>
<td>13.33</td>
<td>13.14</td>
<td>13.70</td>
</tr>
<tr>
<td>EQD2 (Gy), D2cc</td>
<td>10.84</td>
<td>10.75</td>
<td>10.13</td>
</tr>
<tr>
<td>Ratio(D2cc/A AVG Dose)</td>
<td>0.91</td>
<td>0.87</td>
<td>0.97</td>
</tr>
<tr>
<td>Ratio:EQD(D2cc)/EQD(A AVG)</td>
<td>1.18</td>
<td>1.10</td>
<td>1.27</td>
</tr>
</tbody>
</table>
Fx 4-6:
Still high bladder dose
Sufficient target shrinkage

Fx 4-5: 10% reduction
Fx 6: 20% reduction
Reduce bladder dose
Maintain target coverage

Courtesy of C. Bertelsman
Conclusions

• We have described a technique for MRI-based brachytherapy of cervix cancer patients:
  – Multi-sequence: T2W, DW-ADC, and PDW para-sagittal acquisitions
  – Improved visualization of OARs, GTV, and applicator
  – Dose adaptation

• We have described this technique in the context of GEC-ESTRO guidelines and published literature with key differences in:
  – MR image acquisition technique
    • Target definition
    • Applicator reconstruction
  – Dose adaptation