Image-Guided and Adaptive Radiotherapy

PMH 50th Conference

A. Fyles
Dept. of Radiation Oncology
Princess Margaret Hospital
IMRT for Cervix Cancer
Challenges in IMRT for Cervix Cancer

Target Identification
- MR vs CT
- Nodal targets
- Online image quality

Organ motion
- Influence of
  - Bladder filling
  - Rectal filling
  - Normal uterus position

Workload
PMH CTV Definition

- CTV = GTV (+0.7cm margin) + Cervix + parametria + lower 2cm uterus + upper 2cm vagina

- Nodal CTV as per Taylor et al

- Normal Organs at Risk
  - rectum, bladder, sigmoid, bowel, bone etc.
## Point of Interest Analysis in 16 Patients – Mean Values

<table>
<thead>
<tr>
<th>UB = Uncertainty Bounds (confidence limits)</th>
<th>Cranio-Caudal (mm)</th>
<th>Ant-Post (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Intra</td>
</tr>
<tr>
<td>Fundus UB</td>
<td>36.9</td>
<td>9.6</td>
</tr>
<tr>
<td>Os UB</td>
<td>14.8</td>
<td>3.6</td>
</tr>
</tbody>
</table>
Adapting to Change

- Tumors are heterogeneous
- Position changes
  - Inter-fraction, Intra-fraction
- Size and shape changes
- Biology changes
Tumour Shrinkage & Deformation

- Influence of:
  - Tumour factors
    - Biology
      - Hypoxia
  - Treatment factors
    - Chemo-radiation
Adaptive Image-Guided RT

- Complex dynamics of OAR & target motion
- Concerns:
  - Margins?
  - Geographical miss
  - ↑ dose to normal tissues
- *What you see* is not *What you get*
- Adaptive approach is needed for treatment of intact cervix cancer
IMRT Lymph Node Plan

Role for image-guided nodal targeting using USPIO MR
2 cm radial expansion around iliac vessels

Lymph node group | Recommended margins*
--- | ---
Common iliac | 7-mm margin around vessels; extend posterior and lateral borders to psoas and vertebral body
External iliac | 7-mm margin around vessels; extend anterior border by additional 10-mm anterolaterally along iliopsoas muscle to include lateral external iliac nodes
Obturator | Join external and internal iliac regions with 18-mm-wide strip along pelvic sidewall
Internal iliac | 7-mm margin around vessels; extend lateral borders to pelvic sidewall
Presacral | 10-mm strip over anterior sacrum

Shih, 2005
Taylor, 2005
LN Movement During RT

4 mm PTV expansion encompasses >90% of LN movement

Coverage of Unified nCTV7

M. Milosevic, PMH-RMP IGRT, 25/1/2008
Delivered vs. Planned Dose

Image at T=0  →  Mesh-Based Biomechanical Model  →  Image at T=1

- Motion
- Deformation
- Dose accumulation
- Adaptive re-planning

MORFEUS

Slide c/o Kristy Brock
Nominal Plan

Dose Accumulated Plans

Acc Dose wk2
Acc Dose wk3
Acc Dose wk4
Acc Dose Wk5

Adaptive Re-plan

Baseline
Week 1
Week 2
Week 3
Week 4
Week 5

CT_0
MRI_0
MRI_1
MRI_2
MRI_3
MRI_4
MRI_5

Contours
Contours
Contours
Contours
Contours

Surface Meshes
Surface Meshes
Surface Meshes
Surface Meshes
Surface Meshes

Orbit
Initial IMRT strategy – 10 pts

- **LM (large margin) plan**
  - 1-2 cm PTV margin
  - Expectation
    - little OAR sparing
    - Target always covered

- **SM (small margin) plan**
  - 0.5 cm PTV margin
  - Expectation
    - Some OAR sparing
    - Target missed
Initial IMRT strategy – 10 pts

- **Adaptive re-plan**
  - Union CTV of 1st 3 image sets (iCTV)
  - Expectation
    - More OAR sparing
    - Target coverage better

- **Results**
  - LM plan covered *most* pts
  - SM plan seemed adequate for more pts than expected
  - Re-plan did not spare as much OAR as hoped

- **WHY?**
WHY?

- Large CTV – tumour shrinkage did not influence treatment volume as much as expected
- Organ motion – iCTV – resulted in even larger CTVs than baseline
- Estimates of 3D margins too generous based on previous POI data
- Influence of bladder / rectal filling
  - Heterogeneous despite bowel & bladder prep
  - Caused large displacements in CTV location in some pts
- Influence of uterus position

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2nd Adaptive strategy – 25 pts

- Use of ultra-small PTV margins (0.3cm)
- Assume perfect set-up daily (CBCT)
- Separate out pts into consistent & variable bladders
- Adaptive re-plan – after 2nd wk treatment, use only imaging at that time point, no union CTV.
98% of the PTV to be covered by the 95% isodose for all plans

Plan evaluation criteria:
98% of GTV received 5000cGy; 98% HRCTV received ≥ 4900cGy

Dose Accumulation with Inter-Fraction Motion Applied

<table>
<thead>
<tr>
<th></th>
<th>Nom SM</th>
<th>Acc SM</th>
<th>Acc AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTV (D98)</td>
<td>5036</td>
<td>5014</td>
<td>5031</td>
</tr>
<tr>
<td>HRCTV (D98)</td>
<td>4923</td>
<td>4858</td>
<td>4909</td>
</tr>
<tr>
<td>Rectum (V45)</td>
<td>54</td>
<td>51</td>
<td>41</td>
</tr>
<tr>
<td>Sigmoid (V45)</td>
<td>59</td>
<td>61</td>
<td>39</td>
</tr>
<tr>
<td>Bladder (Mean)</td>
<td>4002</td>
<td>4103</td>
<td>3963</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th></th>
<th>Nom SM</th>
<th>Acc SM</th>
<th>Acc AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTV (D98)</td>
<td>5024</td>
<td>4987</td>
<td>5008</td>
</tr>
<tr>
<td>HRCTV (D98)</td>
<td>4911</td>
<td>4783</td>
<td>4780</td>
</tr>
<tr>
<td>Rectum (V45)</td>
<td>52</td>
<td>50</td>
<td>41</td>
</tr>
<tr>
<td>Sigmoid (V45)</td>
<td>61</td>
<td>67</td>
<td>51</td>
</tr>
<tr>
<td>Bladder (Mean)</td>
<td>4065</td>
<td>3960</td>
<td>3930</td>
</tr>
</tbody>
</table>

P < 0.05 compared to Nominal SM plan
Conclusions of MR Study

- Tumour & organ dynamics within the pelvis is complex
- Inter-fraction motion is a major issue in cervix cancer, supporting IGRT
- Small inter-fraction and LN motion/deformation
- Tumour regression during treatment suggests adaptive IGRT
- Conventional plan $\neq$ Delivered dose
- Daily image-guidance and adequate bladder prep is essential
- Adaptive strategy may be successful for some patients
Cervical Stump Carcinoma

- 45 year old woman, previous sub-total hysterectomy for fibroids
- MR
  - 6 cm. tumor replacing cervix, small pelvic nodes
  - sigmoid looped over over tumor
IMRT Boost Treatment

- 5-10% of patients - unsuitable for brachytherapy
- Cervical stump
- Sidewall or nodal disease that receives less than 60 Gy (EBRT and IC)
- PMH IMRT dose of 25.2 Gy in 14 fractions

- Boost to 70 - 75 Gy
- Gross nodal disease may be treated to 65-70 Gy
- Other means of radiation boost
  - Standard EBRT
    - Limited by normal tissue tolerance (dose of 60-65 Gy)

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IMRT Boost - Issues

• Boost Volume
  • Cervix alone – simulating IUA brachytherapy
  • Cervix and pelvic sidewall(s)

• Organ movement.
  • Including bladder and rectal preparation
• Set-up reproducibility
• Immobilization

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IMRT Boost Spares Normal Organs

- Bladder/Rectum
- Femoral heads

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Para-aortic Radiation

- Positive pelvic nodes and/or small PAN or recurrence
- Concurrent cisplatin
- Risk of toxicity GI, hematologic
Para-aortic Radiation with Simultaneous Integrated Boost

Kidneys/Small Bowel
Post-Operative Adjuvant Pelvic IMRT

- Recent RTOG Phase II trial of feasibility
- Toxicity decreased esp. GI
- Possible benefit if chemo-radiation
- Target motion issues minimized with ITV (simulation bladder empty and full)
- Cone-beam imaging for bone matching
MR Image-Guided Brachytherapy for Cervix Cancer

- Adapt to changing volume
- **IR-CTV:**
  - Tumor at diagnosis
  - 20 Gy
- **HR-CTV:**
  - Residual tumor at BT
  - 40 Gy from BT
- Reduced toxicity
- Identification of “non-responders”

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Image-Guided Brachytherapy
Std brachytherapy is not optimal for all patients

HR-CTV
20 patients
Standard plans
MR-dosimetry
(Zwahlen)

V$_{100}$
Image-Guided Brachytherapy

HR-CTV
20 patients
Standard plans

MR-dosimetry (Zwahlen)

Rectum

Dose (cGy)

Rectal wall volume (cm³)

D2cm³
## Optimized IG-Brachytherapy

### Optimization

- 20 cases
- HR-CTV ≥ 40 Gy
- IR-CTV > 20 Gy
- Point A ≤ 40 Gy

<table>
<thead>
<tr>
<th>OAR</th>
<th>Tumor size</th>
<th>Conventional (Gy)</th>
<th>Optimized (Gy)</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sigmoid colon</strong></td>
<td>All tumors</td>
<td>25 ±8.7</td>
<td>22 ±6.6</td>
<td>-14%*</td>
</tr>
<tr>
<td></td>
<td>Small</td>
<td>26 ±3.2</td>
<td>19 ±5.7</td>
<td>-32%*</td>
</tr>
<tr>
<td></td>
<td>Large</td>
<td>25 ±7.4</td>
<td>24 ±6.7</td>
<td>-3%</td>
</tr>
<tr>
<td><strong>Rectum</strong></td>
<td>All tumors</td>
<td>16 ±6.2</td>
<td>16 ±6.7</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Small</td>
<td>16 ±7.8</td>
<td>14 ±7.6</td>
<td>-14%*</td>
</tr>
<tr>
<td></td>
<td>Large</td>
<td>17 ±4.5</td>
<td>19 ±4.5</td>
<td>+14%*</td>
</tr>
<tr>
<td><strong>Bladder</strong></td>
<td>All tumors</td>
<td>31 ±9.2</td>
<td>30 ±9.8</td>
<td>-2%</td>
</tr>
<tr>
<td></td>
<td>Small</td>
<td>30 ±8.7</td>
<td>26 ±9.6</td>
<td>-12%*</td>
</tr>
<tr>
<td></td>
<td>Large</td>
<td>32 ±9.9</td>
<td>34 ±8.6</td>
<td>+6%</td>
</tr>
</tbody>
</table>

*Daniel Zwahlen, 2007*
Optimized IG-Brachytherapy

145 patients
T1b/2a 15%
T2b/3a 59%
T3b 26%

Late Toxicity
Gr. 3-4 GI 4%
GU 4%
Vaginal 5%

Local control
CSS
OS

M. Milosevic, PMH-RMP IGRT, 2008

Potter, 2007
Optimized IG-Brachytherapy

145 patients
T1b/2a 15%
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Gr. 3-4 GI 4%
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Local Control

Small tumors
Large tumors

M. Milosevic, PMH-RMP IGRT, 2008

Potter, 2007
What Next?

- Work by our group & others
  - poor correlation between rectal & bladder volumes and cervix position
- Look at influence of uterus position on target motion
- Simple class solution / margin recipe unlikely given complexity of target motion & deformation
- Contouring nomenclature & guidelines (e.g. GEC-ESTRO and Post-op RTOG)
  - International collaboration – RTOG group in June 08
- Any adaptive strategy needs to be individualised
- At present IMRT not ready for intact cervix

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What next?

- Validate modeled findings with independent cohort of pts with more frequent imaging
  - 2-3 MR scans per wk
  - Initial bladder full & bladder empty MRIs
  - CBCT during treatment
- Explore feasibility of contouring on CBCT images
- Ultimate goal – propose prospective adaptive IMRT strategy for cervix patients

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Radiation Oncology: M. Milosevic, K. Lim, P. Chan, D. Zwahlen, R. Dinniwell, W. Levin, L. Manchul
Medical Imaging: M. Haider
Radiotherapy: V. Kelly, J. Paterson
Biostatistics: M. Pintilie, G. Lockwood

RaySearch Laboratories AB
A. Lundin, H. Rehbinder, J. Löf

Supported by:
National Cancer Institute of Canada through the Terry Fox Run
Giovanni and Concetta Guglietti Family Trust