Target Delineation: Gynecologic IMRT

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Gynecologic IMRT

Growing in popularity

2002 IMRT Survey- 15% respondents using IMRT in gynecology patients

2004 IMRT Survey- 35% using IMRT in gynecology patients


Mell LK, Mundt AJ. Survey of IMRT Use in the USA- 2004 *Cancer* 2005;104:1296
## IMRT Practice Survey (2004)

<table>
<thead>
<tr>
<th>Site</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>85%</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>80%</td>
</tr>
<tr>
<td>CNS Tumors</td>
<td>64%</td>
</tr>
<tr>
<td>Gynecology</td>
<td>35%</td>
</tr>
<tr>
<td>Breast</td>
<td>28%</td>
</tr>
<tr>
<td>GI</td>
<td>26%</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>20%</td>
</tr>
<tr>
<td>Lung</td>
<td>22%</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>16%</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>12%</td>
</tr>
</tbody>
</table>

*Mell LK, Mundt AJ. Survey of IMRT Use in the USA- 2004 Cancer 2005;104:1296*
Gynecologic IMRT
Rationale

• Improved delivery of conventional doses
  – ↓Dose to normal tissues
  – Small bowel, bladder, rectum, marrow

• Dose escalation in high risk patients
  – Node positive
  – Gross residual disease

• Replacement for Brachytherapy
Gynecologic IMRT

• Strong evidence supporting IMRT

• Dosimetric studies have demonstrated its superiority over conventional techniques, particularly in normal tissue sparing
  – Small bowel, bladder, rectum, femoral heads, and bone marrow
1st gynecology IMRT study
10 patients
Compared IMRT vs 3DCRT plans
Volume of small bowel receiving the prescription dose reduced by a factor of 2
Volume of bladder and rectum also reduced by 23%

Dosimetric Pelvic IMRT Studies

Roeske et al. *IJROBP* 2000;48:1613
Chen et al. *IJROBP* 2001;51:332
Ahamad et al. *IJROBP* 2002;54:42
Heron et al. *Gynecol Oncol* 2003;91:39
Wong et al. *IJROBP* 2005;61:830
Cozzi et al. *Radiother Oncol* 2008;89:180
Mell et al. *IJROBP* 2008;71:1504
Bouchard et al. *IJROBP* 2008;71:1343
Igdem et al. *Eur J Gynecol Oncol* 2009;30:547
Yang et al. *Acta Oncol* 2010;49:230
# Intensity Modulated Pelvic RT Planning Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Bowel</th>
<th>Bladder</th>
<th>Rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roeske</td>
<td>↓50%</td>
<td>↓23%</td>
<td>↓23%</td>
</tr>
<tr>
<td>Ahamad</td>
<td>↓40-63%*</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Chen</td>
<td>↓70%</td>
<td>↓**</td>
<td>↓**</td>
</tr>
<tr>
<td>Selvaraj</td>
<td>↓51%***</td>
<td>↓31%***</td>
<td>↓66%***</td>
</tr>
</tbody>
</table>

*dependent on PTV expansion used
**data not shown
***reduction in percent volume receiving 30 Gy or higher

Roeske et al. *Int J Radiat Oncol Biol Phys* 2000;48:1613
Ahamad et al. *Int J Radiat Oncol Biol Phys* 2002;54:42
Heron et al. *Gynecol Oncol* 2003;91:39-45
Chen et al. *Int J Radiat Oncol Biol Phys* 2001;51:332
Dosimetric IMRT Studies

Benefits also with more comprehensive fields

- **Extended Field RT**
  - Portelance et al. IJROBP 2001;51:261
  - Chen et al. IJROBP 2001;51:232
  - Lian et al. IJROBP 2008;70:935

- **Pelvic Inguinal RT**
  - Beriwal et al. IJROBP 2006;64:1395
  - Garofalo et al. *RSNA* 2002

- **Whole Abdominal RT**
  - Hong et al. IJROBP 2002;54:278
  - Duthoy et al. IJROBP 2003;57:1019
  - Kim et al. *TCRT* 2009;5:369
Dosimetric IMRT Studies

Multiple studies suggest IMRT may represent an alternative to brachytherapy

– Low et al. *IJROBP* 2002;52:1400
– Aydogan et al. *IJROBP* 2006;65:266
– Malhotra et al. *JACMP* 2007;8:2450

Or a beneficial adjunct to brachy

– Duan et al. *IJROBP* 2008;71:765

Duan et al. *IJROBP* (2008)
Clinical Outcome Studies

- Increasing number of outcome studies in gynecology patients undergoing IMRT
- Reductions in acute and chronic toxicities, particularly GI toxicity
## Acute Toxicity

<table>
<thead>
<tr>
<th>Source</th>
<th>Pelvis</th>
<th>Pelvic-Paraortic</th>
<th>Pelvic-Inguinal</th>
<th>Whole Abdominal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>G1 g2 g3</td>
<td>G1 g2 g3</td>
<td>G1 n g2 g3</td>
</tr>
<tr>
<td><strong>GI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mundt (2002)</td>
<td>40</td>
<td>60% 0%</td>
<td>10% 0%</td>
<td></td>
</tr>
<tr>
<td>Chen (2007)</td>
<td>33</td>
<td>24% 0%</td>
<td>12% 0%</td>
<td></td>
</tr>
<tr>
<td>Beriwal (2006)</td>
<td>47</td>
<td>70% 0%</td>
<td>4% 0%</td>
<td></td>
</tr>
<tr>
<td>Tierney (2007)</td>
<td>14</td>
<td>57% 0%</td>
<td>21% 0%</td>
<td></td>
</tr>
<tr>
<td>Hsieh (2009)</td>
<td>10</td>
<td>NS 10%</td>
<td>NS 0%</td>
<td></td>
</tr>
<tr>
<td>Zhou (2007)</td>
<td>21</td>
<td>NS 0%</td>
<td>NS 0%</td>
<td></td>
</tr>
<tr>
<td>Hasselle (2010)</td>
<td>111</td>
<td>45% 2%</td>
<td>16% 0%</td>
<td></td>
</tr>
<tr>
<td><strong>GU</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvic-Paraortic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salama (2006)</td>
<td>13</td>
<td>84% 0%</td>
<td>7% 0%</td>
<td></td>
</tr>
<tr>
<td>Beriwal (2006)</td>
<td>36</td>
<td>69% 3%</td>
<td>19% 3%</td>
<td></td>
</tr>
<tr>
<td>Gerszten (2006)</td>
<td>22</td>
<td>10% 0%</td>
<td>10% 0%</td>
<td></td>
</tr>
<tr>
<td>Pelvic-Inguinal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beriwal (2007)</td>
<td>15</td>
<td>20% 6%</td>
<td>13% 0%</td>
<td></td>
</tr>
<tr>
<td>Whole Abdominal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rochet (2010)</td>
<td>10</td>
<td>NS 10%</td>
<td>0% 0%</td>
<td></td>
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</tbody>
</table>
**Chronic Toxicity**

<table>
<thead>
<tr>
<th>Pelvis</th>
<th>GI</th>
<th>GU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>g2</td>
</tr>
<tr>
<td>Mundt</td>
<td>35</td>
<td>2.8%</td>
</tr>
<tr>
<td>Chen</td>
<td>33</td>
<td>0%</td>
</tr>
<tr>
<td>Beriwal</td>
<td>47</td>
<td>0%</td>
</tr>
<tr>
<td>Chen</td>
<td>54</td>
<td>NS</td>
</tr>
<tr>
<td>Hasselle</td>
<td>111</td>
<td>10%</td>
</tr>
<tr>
<td>Kidd</td>
<td>135</td>
<td>------Grade 3-4 GI/GU = 6%------</td>
</tr>
</tbody>
</table>

**Pelvic-Paraortic**

| Beriwal                 | 36     | 2.7% | 5.5% | 0% | 0% |

Mundt et al. Red J 2003;56:1354
Chen et al. Red J 2007;67:1438
Beriwal et al. Gyne Oncol 2006;102:1395
Beriwal et al. Red J 2006;64:1395
Chen et al. Cancer J 2008;14:200
Hasselle et al. Red J (in press)
Kidd et al. Red J (in press)
IMRT Outcome Studies

Evaluated the impact on acute hematologic toxicity

- Several report low rates in patients undergoing concomitant chemoradiotherapy
  - Brixey et al. *IJROBP* 2002;52:1388
  - Mell et al. *IJROBP* 2006;66:1356
  - Lupe et al. *IJROBP* 2007;67:110

- Others studies less favorable

Majority have not intentionally included bone marrow in the inverse planning process
Tumor Control

- Data remain limited
- Increasing number of single institution series published
- Cooperative groups performing clinical trials
# Cervical Cancer

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>FU</th>
<th>Stage</th>
<th>DFS</th>
<th>Pelvic Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intact Cervix</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kochanski</td>
<td>44</td>
<td>23 m</td>
<td>I-IIA</td>
<td>81%</td>
<td>93%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IIB-IIIB</td>
<td>53%</td>
<td>67%</td>
</tr>
<tr>
<td>Beriwal</td>
<td>36</td>
<td>18 m</td>
<td>IB-IVA</td>
<td>51%</td>
<td>80%</td>
</tr>
<tr>
<td>Kidd</td>
<td>135</td>
<td>22 m</td>
<td>IA2-IVB</td>
<td>70%</td>
<td>86.7%</td>
</tr>
<tr>
<td>Hasselle</td>
<td>89</td>
<td>27 m</td>
<td>I-IIA</td>
<td>69.8%</td>
<td>94.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IIB-IVA</td>
<td>51.4%</td>
<td>70.8%</td>
</tr>
<tr>
<td><strong>Postoperative Cervix</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kochanski</td>
<td>18</td>
<td>21 m</td>
<td>I-II (node+)</td>
<td>79%</td>
<td>94%</td>
</tr>
<tr>
<td>Chen</td>
<td>35</td>
<td>35 m</td>
<td>I-II (node+)</td>
<td>NS</td>
<td>93%</td>
</tr>
<tr>
<td>Hasselle</td>
<td>22</td>
<td>27 m</td>
<td>I-II (node +/-)</td>
<td>95.2%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Kochanski et al. *IJROBP* 2005;63:214
Beriwal et al. *IJROBP* 2007;68:166
Chen et al. *IJROBP* 2001;51:332
Kidd et al. *IJROBP* (in press)
Hasselle et al. *IJROBP* (in press)
111 cervical cancer pts
89 intact cervix, 22 postop
Pelvic IMRT +/- Brachy
Median FU = 27 months
Excellent pelvic control
  – IB-IIA intact = 94.7%
  – IIB-IVA intact = 70.8%
  – Postop patients = 100%
Grade ≥ 3 chronic toxicity = 7%

## Endometrial Cancer

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>FU</th>
<th>Stage</th>
<th>DFS</th>
<th>Pelvic Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knab</td>
<td>31</td>
<td>24 m</td>
<td>I-III</td>
<td>84%</td>
<td>100%</td>
</tr>
<tr>
<td>Beriwal</td>
<td>47</td>
<td>20 m</td>
<td>I-III</td>
<td>84%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Knab et al. *Int J Radiat Oncol Biol Phys* 2004;60:303
International Cervical Cancer Radiotherapy Consortium

Peking Union Medical College (Beijing)
Tata Memorial Hospital (India)
AC Camargo Hospital (Brazil)
UC San Diego (USA + Mexico)
University of Chicago (USA)
University of Miami (USA)
Artemis Hospital (India)
Loyola University (USA)
University of Pittsburgh (USA)
University of Iowa (USA)
Moffitt Cancer Center (USA)
King Chulalongkorn University (Thailand)
Istanbul Bilim University (Turkey)
University Hospital Hradec Kealove (Czech Republic)
Far Eastern Memorial Hospital (Taiwan)
Target Delineation

- Step 1 Identify treatment volume
- Depends on the tumor site, disease stage, histology, pathologic features
- Most receive pelvic RT
- More comprehensive volumes in select patients
  - Stage IIIC uterine cancer → EFRT
  - Papillary serous uterine cancer → WART
  - Vulvar cancer → Pelvic-inguinal RT
Target Delineation

• Step 2 Identify individual components of the treatment volume
• More difficult step
• Controversial which components to include
• No consensus even among experts
Target Volume Components
IM-Pelvic RT Patients

Vagina
Upper 1/2
Cervix/uterus (if present)
Parametria tissues
Pelvic Lymph Nodes
Common, internal and external iliacs
Pre-sacral nodes

In all cervical cancer and uterine cancer with cervical involvement
Target Delineation

- Step 3 Decide *how to contour the target*
- Most difficult step

While two physicians may agree on the components of the CTV, they rarely agree on how to contour them
Consensus Guidelines

• Guidelines for target design are being developed

GOG-RTOG-ESTRO-NCIC Target Consensus Meeting
Philadelphia June 2005
Post-hysterectomy CTV
www.rtog.org
RTOG 0418 (Jhingran)

Guidelines based on participants’ opinions and published data
CONSENSUS GUIDELINES FOR DELINEATION OF CLINICAL TARGET VOLUME FOR INTENSITY-MODULATED PELVIC RADIOTHERAPY IN POSTOPERATIVE TREATMENT OF ENDOMETRIAL AND CERVICAL CANCER

WILLIAM SMALL, JR., M.D., * LOREN K. MELL, M.D., † PENNY ANDERSON, M.D., ‡ CARIEN CREUTZBERG, M.D., § JENNIFER DE LOS SANTOS, M.D., ¶ DAVID GAFFNEY, M.D., PH.D., †† ANUJA JHINGRAN, M.D., # LORRAINE PORTELANCE, M.D., ** TRACEY SCHEFTER, M.D., ††† REVATHY IYER, M.D., ‡‡ MAHESH VARIA, M.D., §§ KATHRYN WINTER, M.S., ‡‡‡ AND ARNO J. MUNDT, M.D. ‡‡‡

Red Journal 2008;71:428
Fig. 1. Upper common iliac clinical target volume.

Fig. 2. Mid-common iliac (red) and presacral clinical target volume (blue).
Fig. 3. Lower common iliac (red) and presacral clinical target volume (blue).

Fig. 5. External and internal iliac clinical target volume.
Fig. 4. Upper external and internal iliac (red) and presacral clinical target volume (blue).

Fig. 6. External and internal iliac (red) and parametrial/vaginal (green) clinical target volume.
Fig. 7. Parametrial/vaginal clinical target volume.
LYMPHANGIOGRAM-ASSISTED LYMPH NODE TARGET DELINEATION FOR
PATIENTS WITH GYNECOLOGIC MALIGNANCIES

K. S. Clifford Chao, M.D., and Mary Lin, B.S.
Department of Radiation Oncology, Washington University Medical School, St. Louis, MO

Chao KS et al. Int J Radiat Oncol Biol Phys
2002;54:1147-1152
Fe Oxide nano-particle enhanced MRI

Taken up in benign lymph nodes by macrophages

Target Delineation
Postoperative IMRT

- Only a clinical target volume (CTV) is delineated
- Lymph node regions not delineated with a *symmetric* expansion around vessels
- 0.7 cm margin used to encompass surrounding fat and connective tissues
- 1 cm margin around vaginal cuff
- Normal tissues help define CTV extent
  - Psoas/piriform muscles, bowel and bones
Target Delineation

- Knowledge of normal pelvic anatomy very important

- Poor knowledge of normal anatomy results in poor target delineation
Anatomy

- Ascending colon
- Right psoas
- L5
- IVC
- Aorta
- Cauda Equina
- Left psoas
- Left ureter
- Bowel
- Iliac Crest

[Image of anatomical diagram]
Anatomy

IVC Bifurcation
Right Common Iliac Artery
Left Common Iliac Artery
Descending Colon

Bowel

Psoas L5 Psoas

Ascending Colon

Iliac Crest
Ascending Colon
Psoas Muscle
SI Joint
Right Common Iliac Vein
Right Common Iliac Artery
Left Common Iliac Vein (bifurcating)
Left Common Iliac Artery
Iliacus
Gluteal Muscles
Lumbosacral Nerve Trunk
S1
Anatomy

- Iliac Crest
- Psoas
- Right Common Iliac Vein
- Right External Iliac Artery
- Right Internal Iliac Artery
- S1 nerve root (in pelvic sacral foramen)
- Iliacus
- Bifurcating Vessels
- S2
- Right Common Iliac Vein
Anatomy

- Sigmoid
- Psoas Muscle
- R External Iliac Artery
- R External Iliac Vein
- R Internal Iliac Artery
- R Internal Iliac Vein
- S2
Mons Pubis

Femoral Artery and vein

Urethra

Vagina

Anus

THR
Start CTV contours ~1.5 cm below L4-5 (remember it will be expanded)
CTV is initially small and conical
As vessels bifurcate, it takes on a “bow tie” appearance
Use psoas muscle, small bowel and lumbosacral spine to help define CTV extent.
CTV inferiorly becomes U-shaped, encompassing lateral pelvic nodes and posterior presacral region.
In endometrial cancer pts without cervical extension, *split* the CTV excluding presacral region
Psoas and piriform muscles are helpful
At the level of the vaginal cuff, the CTV takes on a “bow tie” appearance.
Target Delineation
Myself vs Consensus Conference

• I favor inclusion of 1 cm of bladder and rectum in the CTV
• Yes it goes against the CTV concept!
• Provides a more generous margin around the vaginal cuff due to concerns over organ motion*

*Another 0.7 cm expansion is then added to form the PTV
“Integrated Target Volume”

- Creative solution to the organ motion problem developed at MDAH
- Two planning scans: one with a full and one with an empty bladder
- Scans are fused
- *Integrated target volume* (ITV) is drawn on the *full* bladder scan (encompassing the cuff and parametria on both scans)
- ITV is expanded by 0.5 cm → PTV_{ITV}
Small Bowel
Bladder
Integrated Target Volume (ITV)
PTV_{Nodes}

Jhingran A, et al. (MD Anderson)
Endometrial Cancer: Case Study
Chapter 23.2
IMRT: A Clinical Perspective BC Decker 2005
Cautionary Note

Avoid contouring the PTV directly
CTV-PTV is a 3-D expansion!!!
Not always 1 cm on each axial slice

Note the more generous expansion posteriorly (due to the rapidly changing CTV contour)
Inferiorly, the CTV “bow tie” appearance becomes more pronounced.
RTOG Atlas
Much tighter
CTV gradually transitions from a “bow tie” to cylindrical shape
Intact Cervix

• More challenging process
• Much of the problem is that CT is not the ideal imaging approach for such patients
• Some centers insist on MRI
Consensus Guidelines for Delineation of Clinical Target Volume for Intensity-Modulated Pelvic Radiotherapy for the Definitive Treatment of Cervix Cancer

Intact Cervix

• What is needed is a CT-based atlas* for target delineation since obtaining a MRI may be difficult

• MRI is also needed at the time of brachytherapy and two MRIs may not be approved

*under development
UCSD Approach
UCSD Approach
Intact Cervix UCSD Approach

Currently, generating 4 plans for each patient with various asymmetrical margins

- Tight margins (0.5 cm)
- More generous anterior margin (1.2 cm)
- More generous posterior margin (1.2 cm)
- Very generous in all directions (1.5 cm)

At the machine, the best plan is selected for treatment using CBCT

So far, the breakdown is:

- 40% tight margins
- 25% generous anterior
- 25% generous posterior
- 10% very generous in all directions
Planning CT

Central PTV – small margin

Planning PTV (larger margin)

PTV large changes

PTV with posterior margin

PTV with anterior margin
Intact Cervix

• Maybe not ready for prime time

• Focus should be more on the postoperative patient for now
Target Delineation

• Step 4 Identify and contour normal tissues
• Controversial which normal tissues to include
• No consensus even among experts
Normal Tissues

- Normal tissues depend on the clinical case
- In most patients:
  - **Small bowel, rectum, bladder**
- In pts receiving concomitant or sequential chemotherapy, **bone marrow** may be included
- Some centers include the **femoral heads** *
- Kidneys and liver included only if treating more comprehensive fields

*I only do in pelvic-inguinal RT cases*
Normal Tissues

• Be consistent with contouring
  – Helps with DVH interpretation
• Rectum: Outer wall (anus to sigmoid flexure)
• Small bowel: Outermost loops from the L4-5 interspace
  – Include the colon above the sigmoid flexure as well in the “small bowel” volume
• Bone marrow: pelvic bones
Conclusions

Target volume definition is a very important and time-consuming aspect of gynecologic IMRT

Knowledge of normal anatomy and patterns of drainage essential in optimal target delineation
UCSD Center for Advanced Radiotherapy Technologies (CART)