Advances IGRT
Gynecologic Malignancies

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Image-Guided RT (IGRT)

- Image-Guided RT refers to two important aspects of radiotherapy
  - Target Delineation
  - Treatment Delivery

- This presentation will present concepts in IGRT with a focus on gynecologic tumors
IGRT

- **Target Delineation**
  - The use of sophisticated imaging to improve contouring of the target and normal tissues
  - MRI, PET, SPECT, etc.

- **Treatment Delivery**
  - The use of in-room imaging to improve target localization and patient setup
  - In the future, IGRT will be used to adapt treatment to tumor response
New Frontier
Image-Guided Radiotherapy

- Strong rationale in gynecologic tumors, particularly when IMRT is used
  - CT is not ideal for imaging tumors and normal tissues
  - Gynecology patients often difficult to setup
  - Considerable organ motion exists
  - Tumors shrink rapidly
Target Delineation

- Traditional method planar (fluoroscopic) x-rays
- External beam fields based on visualized bony anatomy
- Contrast used to define normal tissues
- Brachytherapy doses prescribed to specified “Points” based on applicator position
2D planning → Poor target coverage and excess normal tissue exposure compared to 3D planning

### CLINICAL INVESTIGATION

**USE OF CT SIMULATION FOR TREATMENT OF CERVICAL CANCER TO ASSESS THE ADEQUACY OF LYMPH NODE COVERAGE OF CONVENTIONAL PELVIC FIELDS BASED ON BONY LANDMARKS**

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43 cervical cancer pts
Evaluated adequacy of coverage of pelvic vessels
Surrogate for lymph nodes
Adequate: >15 mm vessel to block edge

41/43 (95%) inadequate coverage with 2D based fields
24/43 (56%) too generous (> 2 cm)
Excess normal tissue exposure
Beyond CT Imaging

- Interest now focused on more sophisticated imaging for treatment planning
  - Magnetic Resonance Imaging (MRI)
    With ultra-small iron oxide particles (USPIO)
  - Positron Emission Tomography (PET)
    \(^{18}\)F-Deoxyglucose (FDG)
  - Or combined PET/CT units
Fe Oxide nano-particle
Taken up in benign lymph nodes by macrophages

7 mm margin around vessels encompassed 99% of pelvic nodes

FDG-PET particularly useful to identify involved nodes
Boost to higher doses with IMRT

PET+ nodes: 60 Gy/2.4 Gy fx
PET- nodes: 45 Gy/1.8 Gy fx

PET+ Nodes: 59.4 Gy/1.8 Gy fx
PET- Nodes: 50.4 Gy/1.53 Gy fx

Fig. 3. Axial PET and CT images showing a positive PALN and kidneys.
More Advanced Imaging

- Dynamic-Contrast MRI (tumor hypoxia)
  - Cooper et al. Radiother Oncol (2000)
- $^1$H-MR spectroscopy (tumor vs normal tissue)
  - Okada et al. J MRI (2001)

Okada (2001)
Alternative PET Tracers
Metabolic Abnormalities or Hypoxia

- $^{11}$C-Choline (tumor vs normal tissue)
- $^{11}$C-Methionine (amino acid transport)
- $^{60}$Cu-ATSM (hypoxia)

Less uptake in normal tissues

$^{11}$C-Choline imaging
Normal Tissue Delineation

- Novel imaging techniques also valuable for normal tissue delineation

Roeske (2003)
MR-Spectroscopy to identify active (red) marrow sites

Roeske (2005)
SPECT also useful for active bone marrow delineation
T2* Pulse Echo MRI
“Fat Fraction”

Used to differentiate between red and yellow marrow

Information then used to dose paint IMRT plans minimizing red marrow irradiation

Loren Mell MD
UC San Diego
ASCO Young Investigator Award
Image-Guided Target Delineation
Brachytherapy

● Growing interest in using imaging to break away from Point A
● Most attention on MRI

Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy—3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology

Richard Pötter\textsuperscript{a,*}, Christine Haie-Meder\textsuperscript{b}, Erik Van Limbergen\textsuperscript{c}, Isabelle Barillot\textsuperscript{d}, Marisol De Brabandere\textsuperscript{e}, Johannes Dimopoulos\textsuperscript{f}, Isabelle Dumas\textsuperscript{g}, Beth Erickson\textsuperscript{h}, Stefan Lang\textsuperscript{i}, An Nulens\textsuperscript{j}, Peter Petrow\textsuperscript{k}, Jason Rownd\textsuperscript{l}, Christian Kirisits\textsuperscript{m}

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Radiother Oncol (2006)
PET-Guided Brachytherapy

Malyapa

Intravenous FDG
+ FDG inserted into tandem and ovoids
So what do people do?

- IGRT Survey
- 1000 practicing radiation oncologists
- Asked about the use of IGRT technologies for target delineation
- Submitted to ASTRO 2009 and Red Journal

Simpson DR, Mundt AJ, Mell LK
A Survey of IGRT Use in the United States
Submitted to ASTRO 2009
Overall, 94.7% respondents have use sophisticated imaging (> CT) for target delineation.
FDG-PET is clearly most common sophisticated imaging modality for target delineation in gynecology patients

MRI when used, most likely for intracavitary and interstitial brachytherapy planning

Simpson DR, Mundt AJ, Mell LK
A Survey of IGRT Use in the United States
Image-Guided Treatment Delivery
Strong Rationale
Image-Guided Treatment Delivery

- Patient setup is difficult
- Tumors and normal tissues move
- Tumors shrink
Image-Guided Treatment Delivery

Imaging Modalities

Ultrasound
- BAT
- SonArray
- I-Beam
- Restitu

Planar
- EPID
- CyberKnife
- Novalis
- RTRT
- Varian, Elekta

Video
- Video subtraction
- AlignRT
- Photogrammetry

Volumetric
- In-Room CT (FOCAL)
- CT-on-Rails
  - Primatom, EXaCT
- Tomotherapy
- Mobile C-Arm
- Siemens (MVCT)
- Elekta, Varian (kVCT)

IGRT Technologies
Ultrasound-Based IGRT Cervical Cancer

- Little data
- Surprising given popularity in prostate cancer
- But useful for difficult implants

Ultrasound Guidance for Placement of Difficult Intracavitary Implants

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Departments of *Obstetrics and Gynecology and †Radiation and Cellular Oncology, University of Chicago, Chicago, Illinois 60637

Received September 1, 1993
Planar-Based IGRT
Cervical Cancer

- Most studied IGRT approach in cervical cancer
- Long history using electronic portal imaging devices (EPID) to monitor patient setup
- MV image of bony anatomy or implanted markers

Antonuk (2002)
EPID-Based IGRT
Implanted Fiducials on Cervix

Kaatee (2002)
10 cervical cancer pts
Radiopaque tantalum markers on cervix

Used to track cervix position
Image quality good-excellent
½ lost before end of RT
ON-LINE SET-UP CORRECTIONS DURING RADIOTHERAPY OF PATIENTS WITH GYNECOLOGIC TUMORS

JOEP C. STROOM, M.Sc.,† MANOUK J. J. OLOFSEN-VAN ACHT, M.D.,* SANDRA QUINT, B.Sc.,* MERIK SEVEN, B.Sc.,* MARIAN DE HOOG, B.Sc.,* CARIEN L. CREUTZBERG, M.D., PH.D.,* HANS C. J. DE BOER, M.Sc.,† AND ANDRIES G. VISSE, PH.D.†

*Department of Radiation Oncology, †Division of Clinical Physics and Instrumentation, University Hospital Rotterdam, Daniel den Hoed Cancer Center, Rotterdam, The Netherlands

14 gynecology pts
On-line EPID IGRT
Based on boney landmarks
Action level > 4 mm

57% re-positioned
Average time ~ 3 minutes
Acquisition and adjustment

↓PTV margins to 5 mm
Real-Time Tumor Tracking (RTRT)

Four sets of diagnostic x-ray tubes and imagers

1.5 MHU x-ray tube and a fixed floor-mounted collimator

Corresponding ceiling-mounted imager

Mitsubishi Electronics Co Ltd, Tokyo, Japan
http://global.mitsubishielectric.com/
Technical note

High dose three-dimensional conformal boost (3DCB) using an orthogonal diagnostic X-ray set-up for patients with gynecological malignancy: a new application of real-time tumor-tracking system

Ritsu Yamamoto\textsuperscript{a}, Akio Yonesaka\textsuperscript{b}, Seiko Nishioka\textsuperscript{b}, Hidemichi Watari\textsuperscript{a}, Takayuki Hashimoto\textsuperscript{b}, Daichi Uchida\textsuperscript{b}, Hiroshi Taguchi\textsuperscript{a}, Takeshi Nishioka\textsuperscript{b}, Kazuo Miyasaka\textsuperscript{b}, Noriaki Sakuragi\textsuperscript{a}, Hiroki Shirato\textsuperscript{b,*}

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Available online 30 September 2004

10 gynecology patients with implanted fiducials

Necessary CTV-PTV margin using real-time RTRT tracking:
6.9 mm (right-left), 6.7 mm (sup-inf), 8.3 mm (ant-post)

No data using other popular planar systems (CyberKnife, Novalis)
30 patients with isolated PA recurrences

33-45 Gy in 3 fractions using the CyberKnife System with implanted fiducials

Concomitant chemo

Simple immobilization

Alpha Cradle

Four belts to reduce Respiratory Motion
Major predictors of local control (PTV size and PET response)
- 100% if PTV < 17 cc, 91% if CR at 4 months on PET

Low rate of acute and chronic toxicities
- 6 grade 3 or higher acute (5/6 were hematologic)
- Only 1 severe late (ureteral stricture)
Planar-IGRT Systems

- Several vendors have mounted kV sources on gantry opposite amorphous silicon (aSi) flat panel detectors
- Capable of generating high quality kV planar images
- Better image quality and less dose than EPID
- Emerging data using both approaches
- None focused solely on gynecology patients
Commercial Gantry-Mounted Systems
Planar IGRT

Varian On-Board Imaging (OBI)
www.varian.com

Elekta Synergy
www.elekta.com
Planar kV Commercial Systems

Clinical application of image-guided radiotherapy, IGRT (on the Varian OBI platform)

Applications cliniques de la radiothérapie guidée par l'image (RTGI)

Bruno Sorcini and Aris Tilikidis

Department of Medical Physics, Karolinska University Hospital, Stockholm, Sweden

Varian OBI planar-IGRT system
On-line patient setup correction based on bony landmarks
Variety of tumor sites including gynecology
Feasible
Entire process < 1 additional minute
Planar IGRT On-Line Setup
Process Flow
Planar IGRT (Gynecology-Pelvis)

Day 1
MD and RTTs meet at console
Discuss anatomy, special issues, etc.

Day 2 thru Completion

- All shifts ≤ 1 mm
  - Make no shifts and treat

- LR shift > 15 mm
  - SI or AP shift > 15 mm
  - Any concerns
  - Call MD

- Other shifts
  - Make all shifts and treat
Planar kV Commercial Systems

Offer the potential to track Implanted fiducials

Analogous to on-line techniques popularized in prostate cancer

Potentially useful to deliver a high dose conformal boost in patients unable to receive brachytherapy
Volumetric-Based IGRT

- Interest is now turning to **volumetric IGRT**
- Several vendors offer volumetric solutions using the MV treatment beam
  - Tomotherapy, Siemens
- Others generate kV cone-beam CT (CBCT) scans by reconstructing multiple planar kV images
  - Varian, Elekta
Volumetric-IGRT

- High quality kV CBCT scans can be produced
- Useful now to monitor target coverage
- In future, opens door to adaptive RT
On-Line Planar, Off-line Volumetric IGRT  
Cervical Cancer

Planar KV Imaging  
Align boney anatomy  
(↓CTV-PTV margins around Nodes  
Generous margins around cervix)

↓  
Video Imaging  
Monitor Patient Position during Tx

↓  
Volumetric Imaging  
Off-line monitoring of target Coverage  
Adjust margins if necessary
So what do people do?

- IGRT Survey
- 1000 practicing radiation oncologists
- Asked about the use of in-room IGRT technologies for patient setup and tumor localization
- Submitted to ASTRO 2009 and Red Journal

Simpson DR, Mundt AJ, Mell LK
A Survey of IGRT Use in the United States
Overall, 94% respondents use in-room IGRT technologies for patient setup and tumor localization.
<table>
<thead>
<tr>
<th>Modality</th>
<th>All Sites</th>
<th>Gynecology</th>
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<tbody>
<tr>
<td>Ultrasound</td>
<td>22%</td>
<td>1%</td>
</tr>
<tr>
<td>Video</td>
<td>3%</td>
<td>0.3%</td>
</tr>
<tr>
<td>EPID</td>
<td>63%</td>
<td>28%</td>
</tr>
<tr>
<td>OBI (kV)</td>
<td>50%</td>
<td>24%</td>
</tr>
<tr>
<td>CyberKnife</td>
<td>10%</td>
<td>3%</td>
</tr>
<tr>
<td>Novalis</td>
<td>11%</td>
<td>0%</td>
</tr>
<tr>
<td>Tomotherapy</td>
<td>17%</td>
<td>12%</td>
</tr>
<tr>
<td>CBCT (kV/MV)</td>
<td>37%</td>
<td>19%</td>
</tr>
<tr>
<td>CT-on-Rails</td>
<td>4%</td>
<td>1%</td>
</tr>
</tbody>
</table>

- EPID and kV OBI are the most common modalities used in both gynecology and patients in general.
- Next most common modality is volumetric imaging with tomotherapy (12%) or CBCT (19%).
Image-Guided Adaptive RT
Adaptive IGRT

- Tumors shrink
- And often quite quickly with chemotherapy plus RT
- Shrinkage is a double-edged sword

Reduces the chance of a geographic miss

Reduces the conformity of the original plan
14 cervical cancer patients
MRI prior to RT and after 30 Gy external beam
GTV decreased (on average) by 46%
Decrements in CTV and PTV were 18% and 9%
Does Re-Planning Help?

- Re-optimizing the IMRT plan at 30 Gy improved the sparing of the rectum
- Average rectal volume receiving ≥ 95% of the prescription dose
  - 75 cc (range, 20-145 cc) (No Re-planning)
  - 67 cc (range, 15-106 cc) (Re-planning)
  - $P = 0.009$
- Improved bowel sparing seen in women with bulky (> 30 cc) tumors
But what about the subsequent days?

- 10 intact cervical cancer patients treated with IMRT
- Daily CBCT throughout treatment
- Re-planned mid-treatment and evaluated the dosimetric consequences for the remainder of the treatment

Lawson JD, Simpson DR, Mundt AJ, Mell LK
Adaptive Radiotherapy in Cervical Cancer: Dosimetric Analysis Using Daily CBCT
Submitted to ASTRO 2009
**Re-Planning Study**

- Significant improvements in CTV coverage and conformity index
- Significant reductions in the V100 for the small bowel and bladder
- No benefit overall for the rectum
- In fact, 3/10 women significantly worse
- Rectal sparing if new plan adopted
- Suggests that intermittent re-planning may not be optimal
Adaptive IGRT
Gynecologic Tumors

- Currently analyzing a large dataset of daily CBCT in cervical cancer patients undergoing IMRT and chemotherapy

- Daily imaging data allows us to not only ask whether re-planning helps, but the optimal frequency and timing of re-planning
Adaptive IGRT

- Many technical obstacles stand in the way of adaptive IGRT, particularly if performed on-line
- New software tools: image deformation and automated segmentation
- Better quality CBCT imaging
- New rapid, accurate QA approaches
Adaptive IGRT

- Once technical obstacles are overcome, numerous clinical questions remain
  - Does adaptive IGRT help? Does it hurt?
  - Should it be performed on-line or off-line?
  - How often should it be done? Weekly? Daily?
- Such questions can only be addressed in carefully designed clinical trials
Adapt to

What?

Bladder

Tumor

Rectum

Week 1

Bladder

Tumor

Rectum

Week 3

Week 1

Week 3
Adaptive IGRT Strategies

- On-Line Re-Planning
  - The Full Monty done really fast
  - Or Short Cuts (Deform Dose Distribution)

- On-Line Pre-Planning
  - Develop a library of plans in advance
  - “Check out” the plan of the day on-line
On-Line Re-Planning

- Necessary tools being developed
- Multi-million dollar collaborative grant
- Some computations sped up over 500,000x
On-Line Pre-Planning

CT Simulation

Image Deformation

Deformed CTs

Inverse Planning

Treatment Plans

Selection of Appropriate Treatment Plan

CBCT1

Image Deformation

CBCT1 PTV1

Repeat

CBCT2

CBCTn
Machine Learning

- Powerful tool
- Not been applied to radiation oncology
- Enormous potential uses
- Could obviate many tedious, time-consuming steps
Machine Learning
Rapid Interpretation of 3D Image

Anger  Fear  Sad  Disgust  Joy  Surprise

http://www.cs.cmu.edu/afs/cs/user/ytw/www/facial.html
Machine Learning
Rapid Interpretation of 3D Image

Yes
Use Plan 17

Yes
Use Plan 3

No

Yes
Use Plan 12

No

Yes
Use Plan 7

Adapt???