Transition from 2D to 3D Brachytherapy in Cervical Cancers: The Vienna Experience

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Disclosures

Richard Pötter, MD, does not have any financial relationships or products or devices with any commercial interest related to the content of this activity of any amount during the past 12 months.

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Driving forces for the evolution from point (A) to 3D/4D image guided adaptive approach

Improvement of local control in advanced disease
   Improvement of cure

Decrease of adverse side effects/improvement in QoL
   (rectosigmoid, bladder, vagina, bowel, fatigue…)

Not accepting the „mystery“ of point A-based intracavitary brachytherapy

Implementation of 3D/4D Radiotherapy into Gynaecol.

2D Image based brachytherapy (100 years)

Clinical examination
3D/4D drawing
Applicator insertion
Standard dose plan
Dose delivery
Clinical Evaluation

Vienna 1918
Painting

Adler: Strahlentherapie 1918

Radiography

MRI Since 1998

CT since 1983

Image-guided adaptive Brachytherapy

Repetitive Imaging
application of EBRT/Brachytherapy
Applicator insertion

3D/4D imaging

Repetitive clinical examination
+ 3D/4D drawing

Contouring

Applicator Reconstruction

3D dose planning

Dose delivery
EBRT from 2D to 3D
Avoidance of "geographical miss"
* posterior field border
* anterior field border

Gerstner et al. R&O 1999
Zunino et al. IJROBP 1999

Technology Development: Higher conformity through IMRT
Better sparing of OAR (bowel/bladder)
Higher chance for geographical miss
Treatment Planning 2D vs 3D
In Brachytherapy

Point A (since 1938)
Point A / target dose

D90 = 65 Gy

Point A / target dose

D90 = 90 Gy
Standard loading pattern

Optimized loading pattern
Standard loading pattern

Optimized loading pattern
Pattern of tumor regression:
up to mid parametrium

Kirisits et al.
IJROBP 2006

Dimopoulos et al.
IJROBP 2007

The Vienna Applicator

Median volume = 32 cm³  75 patients

HR-CTV D90 standard

Target dose (Gy)
60 70 80 90 100 110 120

Sigmoid dose
40 50 60 70

85 Gy

EQD2 α/β=10Gy

Dose constraint

Violation of OAR constraint

Tanderup 2007/2010
Median volume = 32 cm³  75 patients

Optimised

85 Gy
EQD2α/β=10Gy
Dose constraint

Imaging And Target Definition
Stage IIB Target Definition

At diagnosis
Pathology and Topography
Stage IIB
Tumour Cervix Uterus Parametria Organs at Risk

Change of GTV and CTV with time (4D RT)

At brachytherapy
Pathology and Topography
Contouring and Dose Volume Assessment

MRI: Initial tumour extension (3D RT) pattern of response (4D RT) for adaptive MRI based planning

Dimopoulos et al., Strahlentherapie 2009
BT-Preplanning in cervical cancer:
Different imaging modalities Max Schmid, Vienna University

Target delineation on CT with help of MRI and 3D clinical examination
(Federico et al. ABS 2012)

Analysis with respect to the overall study cohort:

<table>
<thead>
<tr>
<th>Volume [ccm]</th>
<th>CT/MR volume ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>Median</td>
</tr>
<tr>
<td>HR-CTV1</td>
<td>57.62</td>
</tr>
<tr>
<td>HR-CTV2</td>
<td>46.19</td>
</tr>
<tr>
<td>HR-CTV3</td>
<td>37.55</td>
</tr>
<tr>
<td>HR-CTV MRI</td>
<td>30.89</td>
</tr>
</tbody>
</table>

Normalized median volume reduction:
- HR CTV FIGO: \( \sim 32\% \) \( p \leq 0.05 \)
- HR CTV Clinical Drawings: \( \sim 17\% \) \( p \leq 0.05 \)
- HR CTV Pre-BT MRI:
3D Dose Reporting
And Clinical Outcome

Overview of adaptive target concepts in cervix cancer

ICRU/GEC ESTRO report 88
under publication
Fig. 5.9-11
Cumulative Dose Volume Histograms for GTV, HR CTV, IR CTV for 45 Gy EBT (1.8 Gy/f) and 4x7 Gy HDR BT in HR CTV*

*Dose per fraction [Gy]

D90, D98, D50

Vol [%]

GTV, HR CTV, IR CTV

Total dose \(\alpha/\beta=10\) Gy

3D based dose volume constraints OAR

- Classical Maximum Dose
- In 3D no clinical relevant endpoint

- fixed volume ~ tolerance dose (total dose)
  - „minimum dose to the most exposed tissue“*
  - 0.1 cc: 3D „maximum dose“: ulceration (fistula)

0.1 cc: 3D “maximum dose”: ulceration (fistula)

1 cc/2 cc: teleangiectasia
(20 mm x 20 mm x 5 mm)

2 cm³

0.1 cm³

(">5 cc: fibrosis endpoint")

*GYN GEC ESTRO Recommendations (II) Radioth. Oncol. 2006
Cumulative Dose Volume Histograms for Bladder, Sigmoid, Rectum for 45 Gy EBT (1.8 Gy/f) and 4x7 Gy HDR BT in HR CTV*

represents the minimal dose for the most irradiated Volume of x cm³

*GYN GEC ESTRO Recommendations (II) Radioth. Oncol. 2006

LOCAL CONTROL - CLINICAL DATA
DOSE AT POINT A vs. D90 IN IMAGE BASED HR-CTV

<table>
<thead>
<tr>
<th>EARLY DISEASE</th>
<th>DOSE Pt A / D90 HR</th>
<th>BEST STANDARDS</th>
<th>AIM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>75 Gy / 95+ Gy</td>
<td>90-95%</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ADVANCED DISEASE</th>
<th>DOSE Pt A / D90 HR</th>
<th>BEST STANDARDS</th>
<th>AIM</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIB&lt;5cm</td>
<td>80 Gy / 90+ Gy</td>
<td>70-85%</td>
<td>95-100%</td>
</tr>
<tr>
<td>IIB/IIIB&gt;5cm</td>
<td>85 Gy / 85+ Gy</td>
<td>50-65%</td>
<td>85-90%</td>
</tr>
</tbody>
</table>

Expected Improvement through Image Guided Adaptation:
5-40%: IB: 5-10%; II B lim: 10-20%; IIb ext, III B: 20-40%
MRI based Treatment Planning

- **Major Learning Period: 98-2000** (73 consecutive patients)
  - no systematic prospective protocol (point A/ICRU points OAR)

- **Systematic prospective protocol since 2001** (72 consecutive pts.)
  - HR CTV concept
  - GTV, HR CTV + OAR contouring
  - Biological modelling (linear-quadratic model)
  - Dose Volume constraints: OAR (2 cm³): 75/90 Gy(EQD2, α/β=3Gy)
  - Prescription: HR CTV (D90): 85+ Gy(EQD2, α/β=10Gy)

  Intracavitary + interstitial Brachytherapy, if D90 < 85 Gy

  Prospective 3D image based optimisation

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**Linking DVH-parameters to clinical outcome**

**D90 for the HR CTV**

Analysis (n=141, FIGO: IB-IVA, median follow-up=51 months)

- **D90 for the HR-CTV and probability of local control**

  - Entire population (n=141)
  - Tumours > 5cm (n=76)

  **D90 HR CTV 90 Gy EQD2**
  - 90% probability for local control

  **D90 HR CTV 70 Gy EQD2**
  - 65% probability for local control

*Dimopoulos et Radioth & Oncol 2010*
TREATMENT PERIOD (-/+ IGABT) AND TUMOUR SIZE

mean 81 Gy vs. 90 Gy in CTV_{HR}

Pötter R. et al. Radiother Oncol 2007

156 patients MRI guided BT, Vienna 2001-2008, mean D90 to HR CTV 92 Gy
7/156 with G3 and 4/156 G4 toxicity (LENT SOMA) Radioth & Oncol 2011

Pötter et al, Radiotherapy & Oncology, 2011
Dose volume effects for rectal morbidity applying GEC ESTRO recommendations

N = 35 patients with rectosigmoidoscopy

VRS: Vienna Rectoscopy Score

Clinical late Effects LENT SOMA score

Georg et al. Radioth&Oncol 2009

„New“ Paradigm
Image guided adaptive brachytherapy:
Adaptation of target in space (3D) and time (4D)

• macroscopic tumour response
  plus change of overall topography

• adaptation of high risk Clinical Target Volume
  in 3D (space) and 4D (time) [each fraction]

• enables high radiation doses (up to >90 Gy)
  in limited volumes (HR CTV 15-80 ccm)

• prospective application of dose volume constraints 3D/4D
  for high risk CTV and organs at risk [each fraction]