Image guided adaptive brachytherapy in patients with cervical cancer

8. Årsmøde Januar 2013.
Dansk Radiologisk Selskab &
Selskab for klinisk Fysiologi og Nuklearmedicin

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A quick reminder about brachytherapy

- Direct insertion of radioactive sources in tumor/affected organ
- No problem of organ motion
- Steep dose gradient
- High dose to the target
- Sparring of OAR
- Large dose per fraction (high biological effect)
- Reduction of treatment time
2D brachytherapy: Limitations

- NO UNFORTUNATELY NOT!!
PDR-BT: Dose rate during one pulse
Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group* (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV

Christine Haie-Meder\textsuperscript{a,*}, Richard Pötter\textsuperscript{b}, Erik Van Limbergen\textsuperscript{c}, Edith Briot\textsuperscript{a}, Marisol De Brabandere\textsuperscript{c}, Johannes Dimopoulos\textsuperscript{b}, Isabelle Dumas\textsuperscript{a}, Taran Paulsen Hellebust\textsuperscript{d}, Christian Kirisits\textsuperscript{b}, Stefan Lang\textsuperscript{b}, Sabine Muschitz\textsuperscript{b}, Juliana Nevinson\textsuperscript{e}, An Nulens\textsuperscript{c}, Peter Petrow\textsuperscript{f}, Natascha Wachter-Gerstner\textsuperscript{b}

Radiotherapy and Oncology 74 (2005) 235–245
3D image guided procedure

- Applicator insertion
- 3D imaging
- Contouring
- Reconstruction of applicator
- 3D dose planning
- Dose delivery
Contouring

- Contouring in para-transversal T2 images
- Registration to para-coronal and para-sagittal T2 images
MRI-based 4D IGBT: IC optimisation

Standard  →  Optimised

HR CTV

Prescription isodose

Lindegaard 2008
Fig. 2. Dose distribution in a transverse plane (a) at level of point A and (b) in the sagittal view comparing the standard plan from intracavitary alone to combined version. The needles are loaded over a length of 2 cm with 10% dwell weight compared with the source positions inside the tandem and ring.

Kirisits 2006
Needle cap with 12 steering holes for plastic needles
MRI-based 4D IGBT: IC/IS optimisation

Significant dose into sigmoid, rectum and bladder

Prescription isodose

HR CTV

Standard

Optimised

Lindegaard 2008, Tanderup 2011
## Benefit of IGABT – DVH parameters

<table>
<thead>
<tr>
<th></th>
<th>Small tumours (&lt; 32cc)</th>
<th>Large tumours (≥ 32cc)</th>
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</thead>
<tbody>
<tr>
<td><strong>Target covered</strong></td>
<td>94%</td>
<td>14%</td>
</tr>
<tr>
<td><strong>OAR respected</strong></td>
<td>28%</td>
<td>66%</td>
</tr>
<tr>
<td><strong>TRAK</strong></td>
<td>-20%</td>
<td>+2%</td>
</tr>
</tbody>
</table>

- Point A based
- IGABT
- Point A Based
- IGABT

Lindegaard 2008, Tanderup 2011
Multi-institutional data on IGABT in cervical cancer

Results of the FRENCH STIC prospective study

Study design: Non-randomized trial on 2D vs 3D BT

705 Patients

Low stage tumors 2D: N=76
BT+Surgery 3D: N=89

All tumors 2D: N=142
EBRT+BT+Surgery 3D: N=163

Advanced tumors 2D: N=118
EBRT+BT 3D: N=117
Multi-institutional data on IGABT in cervical cancer

Results of the FRENCH STIC prospective study

Local recurrence-free survival

Cumulative toxicity CTAEv3.0

Mono-institutional data on IGABT in cervical cancer

Clinical outcome in 156 patients with cervical cancer treated with EBRT and MRI-based IGABT

Late morbidity (LENT/SOMA)

<table>
<thead>
<tr>
<th>Actuarial morbidity grade 3-5 at 3/5 years</th>
<th>Vienna 1889-2000&lt;sup&gt;B&lt;/sup&gt;</th>
<th>Vienna 2001-2008&lt;sup&gt;C&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Bowel/rectum</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Vagina</td>
<td>31</td>
<td>7</td>
</tr>
</tbody>
</table>

<sup>A</sup> EBRT alone and CT-based BT
<sup>B</sup> EBRT ±chemotherapy and IGABT: Learning period
<sup>C</sup> EBRT ±chemotherapy and IGABT: Protocol period

Pötter et al. Radiother. Oncol. 2011
Mono-institutional data on IGABT in cervical cancer

- **local control (01-08)**
- **cancer specific survival (01-08)**
- **overall survival (01-08)**

- **8 events: 95%**
- **37 events: 74%**
- **49 events: 68%**

Pötter et al. Radiother. Oncol. 2011
141 patients treated with IGABT

- Median follow up 51 months
- 23 bladder events (G2+ LENT/SOMA)
- 11 GI events (G2+ LENT/SOMA)

Georg et al. IJROBP 2012 & 2011, Koom IJROBP 2009
796 registered patients from 12 institutions

<table>
<thead>
<tr>
<th>No. of Centers</th>
<th>Nov. 2009</th>
<th>Nov. 2010</th>
<th>Apr. 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of pts.</td>
<td>111</td>
<td>306</td>
<td>610</td>
</tr>
</tbody>
</table>

- Paris 95
- Århus 75
- Vienna 66
- Ljubljana 49
- London 51
- Utrecht 39
- Mumbai 35
- Arnhem 27
- Leuven 24
- Trondheim 22
- Maastricht 18
- Leeds 25
- Leiden 11
- Kaposvar 11
- Edmonton 20
- Milwaukee 5
- Chandigar 6
- Oslo 1
- Amsterdam 1
- Pamplona 6
Retro-EMBRACE: A MULTICENTRE retrospective study of Image Guided Adaptive Brachytherapy in cervical cancer

Alina Sturdza¹, Lars Ulrik Fokdal², Jacob Christian Lindegaard², Kathrin Kirchheiner¹, Karen Nkiwane¹, Charles Gillham⁵, Christine Haie-Meder⁶, Peter Hoskin⁷, Hilde Janssen⁹, Ina Maria Jurgenliemk-Schulz⁴, Gerry Lowe⁷, Umesh Mahantshetty¹⁰, Renaud Mazeron⁶, Orla Mc Ardle⁵, Christel Nomden⁴, Primož Petrič⁸, Barbara Šegedin⁸, Li Tee Tan¹¹, Ekkasit Tharavichtkul³, Erik Van Limbergen⁹, Christian Kirisits¹, Kari Tanderup², and Richard Pötter¹.

**Table 1. FIGO Stage based local control rate**

<table>
<thead>
<tr>
<th>FIGO Stage</th>
<th>Patient Number</th>
<th>Persistent disease</th>
<th>Local recurrence</th>
<th>% Local control (stage based)</th>
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<tbody>
<tr>
<td>IB</td>
<td>83</td>
<td>0</td>
<td>1</td>
<td>98.8</td>
</tr>
<tr>
<td>IIA</td>
<td>40</td>
<td>1</td>
<td>3</td>
<td>90</td>
</tr>
<tr>
<td>II B</td>
<td>230</td>
<td>9</td>
<td>10</td>
<td>91.8</td>
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<tr>
<td>IIIA</td>
<td>14</td>
<td>1</td>
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<td>85.7</td>
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<tr>
<td>IIIB</td>
<td>69</td>
<td>5</td>
<td>5</td>
<td>85.5</td>
</tr>
<tr>
<td>IVA</td>
<td>13</td>
<td>2</td>
<td>1</td>
<td>76.9</td>
</tr>
<tr>
<td>IVB</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>454</td>
<td>18</td>
<td>21</td>
<td>91.4</td>
</tr>
</tbody>
</table>

**Graph:**
- **D90 HRCTV:** 84 ± 12 Gy
- **Local control rate:** 91.4% at 3 years
- **415/454 patients**
IGABT in other gynaecological tumors?

...Is there a role for image guided adaptive brachytherapy in locally advanced or recurrent gynaecological malignancies?

Brachytherapy

Image and laparoscopic guided interstitial brachytherapy for locally advanced primary or recurrent gynaecological cancer using the adaptive GEC ESTRO target concept

Lars Fokdal a,*, Kari Tanderup a,b, Søren Kynde Nielsen c, Henrik Kidmose Christensen d, Lisbeth Røhl e, Erik Morre Pedersen e, Niels Kim Schønemann f, Jacob Christian Lindegaard a

a Department of Oncology, Aarhus University Hospital, Denmark; b Institute of Clinical Medicine, Aarhus University, Denmark; c Department of Medical Physics; d Department of Surgery; e Department of Radiology; and f Department of Anaesthesiology, Aarhus University Hospital, Denmark

CLINICAL INVESTIGATION

TREATMENT OF LOCALLY ADVANCED VAGINAL CANCER WITH RADIOCHEMOTHERAPY AND MAGNETIC RESONANCE IMAGE-GUIDED ADAPTIVE BRACHYTHERAPY: DOSE-VOLUME PARAMETERS AND FIRST CLINICAL RESULTS

Johannes C. A. Dimopoulos, M.D.,* Maximilian P. Schmid, M.D.,† Elena Fidarova, M.D.,† Daniel Berger, Ph.D.,† Christian Kiriatis, D.Sc.,† and Richard Pötter, M.D.†

*Department of Radiation Oncology, Metropolitan Hospital, Athens, Greece; and †Department of Radiotherapy, Medical University of Vienna, Vienna, Austria
Treatment concept (I)

**EBRT:**
- 3D conformal or IMRT
- 45-50Gy / 1.8-2Gy
- Nodal boost if indicated

**Chemotherapy:**
- Weekly cisplatin in SCC
Treatment concept (II)

Brachytherapy:
- PDR schedule
- MR image guided treatment planning
- GEC-ESTRO recommendations
- Planning aim $D_{90} > 80-85\text{Gy}$ for HR CTV
### Outcome & DVH parameters

<table>
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<tr>
<th></th>
<th>Aarhus</th>
<th>Vienna</th>
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<tr>
<td><strong>Number of pts.</strong></td>
<td>28</td>
<td>13</td>
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<tr>
<td><strong>Followup (month)</strong></td>
<td>18 (6-61)</td>
<td>43 (19-87)</td>
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<tr>
<td><strong>3 months CR (%)</strong></td>
<td>92</td>
<td>100</td>
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<tr>
<td><strong>LC (%)</strong></td>
<td>92 (2Y)</td>
<td>92 (3Y)</td>
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<td><strong>OS (%)</strong></td>
<td>74 (2Y)</td>
<td>85 (3Y)</td>
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<tr>
<td><strong>Morbidity G3+ (%)</strong></td>
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**HRCTV**

- **D100 (Gy)**: 69 (61-80) vs. 71 (55-88)
- **D90 (Gy)**: 82 (77-88) vs. 86 (64-110)

**D2cc**

- **Bladder (Gy)**: 65 (47-81) vs. 80 (55-129)
- **Rectum (Gy)**: 71 (50-77) vs. 70 (46-81)
- **Sigmoid (Gy)**: 52 (44-68) vs. 60 (53-70)
# Interstitial-BT in gynaecological malignancies

<table>
<thead>
<tr>
<th>Author</th>
<th>(N)</th>
<th>EBRT (Gy)</th>
<th>Brachytherapy</th>
<th>Modality</th>
<th>Applicator</th>
<th>Dose (Gy)</th>
<th>CR (%)</th>
<th>OS (%)</th>
<th>DFS (%)</th>
<th>LC (%)</th>
<th>Morbidity G3-4 (%)</th>
<th>Follow-up (years)</th>
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<td>47</td>
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Future directions in IGABT (I)

**RETRO EMBRACE**
An international study on MRI-guided Brachytherapy in locally Advanced Cervical cancer

**EMBRACE**
An international study on MRI-guided Brachytherapy in locally Advanced Cervical cancer

Wait and see 😊

www.embracestudy.dk
www.retroembrace.com
MERIT-study: MEtastatic disease in cervical cancer: The benefit of advanced Radiation treatment combined with Intensive chemoTherapy

Cervical cancer N+, III-IVB

Randomisation

IGART $\geq 85$ Gy

IGART $\geq 85$ Gy + 4x Carboplatin/paclitaxel

www.embracesteudy.dk