SAM Joint Imaging: Advances and Innovations in Image Guided Brachytherapy

Modern Intracavitary Brachytherapy

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Disclosures

Ad-hoc consultant for Varian Corp., Brachytherapy Division

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• Christian Kirisits, DSc, Vienna, Austria
• Astrid de Leuw, PhD, Utrecht, The Netherlands
• Kari Tanderup, Aarhus, Denmark
• Junzo Chino, MD, Adam Olson, MD, Jim Chang, PhD, Duke, NC
Brachytherapy in Gyn Cancer in USA

4-year Cause Specific Survival
64.3% vs 51.5%, P<.001

And Overall Survival
58.2% vs 46.2%, P<.001

This study revealed a concerning decline in brachytherapy utilization over the past decade in the United States and significant geographic disparities in brachytherapy use. Our multivariable analysis of the propensity score-matched cohort, brachytherapy use was independently associated with better CSS and OS.

We postulate that the sharp decline in brachytherapy utilization in 2013 was the result of increased uptake, despite a dearth of published data, of highly conformal radiation therapy techniques including intensity modulated RT (IMRT) and more recently stereotactic body radiation therapy (SBRT). In a 2002 survey of U.S. radiation oncologists, 15% of the respondents reported using IMRT in gynecology patients, by 2004, 35% used IMRT (14, 15).
Brachytherapy has been an essential component in the successful treatment of cervical cancer for more than 100 years.

Repeating painful mistakes from the past
1970s – 25MV, shrinking of EBRT fields to deliver 60-70 Gy in stage IIIB $\rightarrow$ brachy almost eliminated

With poorer survival rates and higher complications, it was abandoned, but it took years.

Prospective trial
Role of MRI guided brachytherapy (IGBT) in locally advanced cervical cancer
correlate image based DVH parameters for the clinical target volume and for organs at risk with outcome.

Courtesy of C. Kirals
Overall Accrual

On 31st December 2015 overall number of registered patients was 1412!

Overall Survival locally advanced cervical cancer
SBRT/IMRT boost vs. 2D BT vs. 4D IGABT

IG(A)BT – key to excellent overall survival rates

- 3D MRI guidance:
  - Possibility to conform the dose given with BT with regard to volume (3D).
  - And time (adaptive component, 4D): Image at each fraction and plan to take into account OARs and tumor regression.
Role of imaging in modern IB

- Application insertion
- Planning
- Treatment Verification
- Applicator design
- Facilitate real-time dosimetry
- Dose summation
- For response

Objectives

- Establish common terminology
  - HDR Intracavitary Brachytherapy
  - Current guidelines – GEC-ESTRO/ABS (pre ICRU 89)
- MRI imaging in IGBT
  - Insertion, planning, verification
  - Hybrid techniques: MRI/CT/CBCT
  - Imaging for applicators design
  - Role in new ICRU 89
LDR vs. HDR

- Several large studies were designed to compare LDR with HDR for cervical cancer
  - Hareyama, 2002 (randomized trial), Japan, ACS
  - Gaur, 2012 (randomized trial), India, Ind J Clin Practice, v. 23, no. 4, 203-211

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No differences between HDR and LDR in OS, local recurrence and late complications

> 2000 patients
Part I & II: Summary

- (Volumetric) Imaging:
  - Localization: radiographic images, CT, MRI
  - CT- and MR-based localization allows for correlation of anatomic data with source positioning.
  - MR best modality for normal tissue and tumors of the uterus and uterine cervix
  - Details for MR sequences adequate for contouring and planning
  - Use of US for applicator placement and cervix delineation

Part I & II: Summary

- Contouring:
  - HR-CTV, IR-CTV, OARs (rectum, bladder, sigmoid)

- Prescription:
  - Target, target dose, dose per fraction, fractionation plan, isotope, dose to OARs, applicator used

- Treatment planning
  - TP and dosimetry SHOULD be performed every time applicators are inserted, even if fixed applicator geometry is used.
  - HR-CTV coverage D90 should equal 100%
  - When using radiographs, prescribe to point A
TP and dosimetry SHOULD be performed every time applicators are inserted, even if fixed applicator geometry are used.

Part I & II: Summary

- Dose calculation and guidelines:
  - Recommended conversion of HDR fractionations into biologically equivalent doses in 2-6 Gy fractions (EQD2)
  - Spreadsheet @ www.americanbrachytherapy.org/guidelines.html
  - Ability to script (API scripting) in BrachyVision (Varian) to convert raw doses into EQD2 (A. Faught et al, Brachytherapy, vol. 15, S1, S137-138) – point doses
  - SW that calculates 3D distribution of biological doses (Velocity, MIM)
Part I & II: Summary

- Recommended reporting

  The ABS recommends for intracavitary:
  1. The type of source.
  2. The prescription point in a defined target volume.
  3. The dose to prescription point A per source.
  4. Total activity per source.
  5. Loading point.
  6. Dose, Plan, and plan path included.

Dose to point A, regardless of imaging modality

  Standard parameters to be reported:
  - D2cc for OARS
  - D90 and D100 (D98), V100 for HR-CTV

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MRI

- MRI: Gold Standard
  - GEC-ESTRO/ABS Guidelines: Defined role of MRI in IGBT
  - MRI better suited for assessing the target (the cervix and any residual disease)


MRI for evaluation and management of cervical cancer

A practical review of magnetic resonance imaging for the evaluation and management of cervical cancer
Proposed Workflows = f (available imaging)

2 Types

- MR in brachy suite:
  - MR guided insertions
  - MR-based (adaptive) planning (MR used at each FX)
  - MR-based treatment verification

- MR outside brachy suite:
  - MR-based (adaptive) planning (MR used at each FX)

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ISABT treatment of advanced Cervical cancer

Standard Clinical Procedure

MR-guided application
- Planner's visit to radiotherapy department
- MR scan for treatment planning
- MR scan for post-treatment
- Verification on treatment plan

Adaptive interventions
- Use of MR to verify treatment plan
- Dose recalibration after adaptive treatment
- Change of trajectory

- Reducing uncertainties in delivering prescribed dose

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Fig. 3: Flow chart of incorporation of MR with the CEC-CT/ICU "gold standard" and 2 electron-based approaches for limited availability with MRI after F pretreatment and MRI prior to treatment planning.
Challenges for MR in Brachy Suite

Stability: Vaginal Balloon Packing

Pre vs. Post Plan, FX1

<table>
<thead>
<tr>
<th></th>
<th>HRCTV</th>
<th>HRCTV</th>
<th>IRCTV</th>
<th>A_Lt</th>
<th>A_Rt</th>
<th>Bladder Dm</th>
<th>Rectum Dm</th>
<th>Sagittal Dm</th>
<th>Bovine Dm</th>
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<tbody>
<tr>
<td>Pre</td>
<td>540</td>
<td>365</td>
<td>330</td>
<td>350</td>
<td>567</td>
<td>376</td>
<td>230</td>
<td>410</td>
<td>280</td>
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<tr>
<td>Post</td>
<td>607</td>
<td>374</td>
<td>331</td>
<td>306</td>
<td>559</td>
<td>376</td>
<td>234</td>
<td>441</td>
<td>314</td>
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<tr>
<td>%</td>
<td>-5.3</td>
<td>2.9</td>
<td>3.4</td>
<td>2.5</td>
<td>2.2</td>
<td>2.4</td>
<td>1.3</td>
<td>7.6</td>
<td>25.6</td>
</tr>
</tbody>
</table>
What to do when:

• Limited Access to MRI: Hybrid Methods
  - MRI + CT
  - MRI + CBCT

• NO access to MRI
  - CT alone
  - CBCT alone
  - US-based

Limited Access: Hybrid Methods

• Use of MRI at least at 1st FX and identify HRCTV/IRCTV

• Continue subsequent fractions with
  - CT
  - CBCT

• Why MRI 1st FX?
• Is the Hybrid Flow an acceptable alternative to MRI for each FX?
Dimopoulos et al. Radiother Oncol Suppl 2004

Tumour regression

The HRCTV volumes displayed variability between fractions (median 47% @planning, 33%), and resulted in variability in the plans developed to meet GEC-ESTRO dose goals.

Use MRI for each FX


Why at least 1 MRI? For HR CTV delineation
**Advanced MRI-based HDR Planning**

3D image guided procedure

Brachy Suite
+/- US

Hybrid (CT/MRI based) vs. MRI only based image-guided brachytherapy in cervical cancer: Dosimetry comparisons and clinical outcome

Te-Rong Cheang,1,3 Peter Bosmans,1,3 Brian Brels Maher,2 Sue Buhk,
Carolyn Richardson,1,3 Rashed Al Qahtani,1 Sarah Swift,1 Jean Orme,1 Rachel Cooper1
1Radiation Oncology, University of Sydney, Sydney, Australia, 2Radiology, University of Sydney, Sydney, Australia, 3Sydney Radiation Oncology, Sydney, Australia

**ABSTRACT:** Limited access to MRI has limited the implementation of MRI-based image-guided brachytherapy (IBT) in the era of 3D conformal radiation therapy. Unlike others, most women who are referred for brachytherapy do not have access to MRI or are not eligible to receive MRI. The ability to image with both CT and MRI has been a key advantage in the use of hybrid image-guided brachytherapy (IBT). In this study, we present our experience of a consecutive group of 14 patients who were treated with the IBT technique between January and April 2014. All patients had a 3D conformal brachytherapy plan fused to the planning CT image and had an additional fractional CT image approximately 3 days after the initial CT image. The second CT image was acquired on the same day as the MRI and was used for the second planning. All patients were treated with a hybrid IBT technique, with CT-based planning and MRI-based verification. All patients had a CT image and a MRI image pre-treatment. The CT and MRI images were fused, and the additional IBT plan was fused to the MRI image. The IBT plan was then verified using MRI-based image-guided brachytherapy.

**RESULTS:** Median follow-up was 41 months (range, 23–71 months). Excellent 3-year local control, overall progression-free survival, and overall survival of 92.6%, 78.8%, and 77.7% were seen with the hybrid approach and 92.2%, 66.3%, and 49.6% with a 3-fraction conformal MRI approach, respectively. Dosimetry achieved and late toxicity rates were comparable in the two groups.

**CONCLUSIONS:** Hybrid IBT in locally advanced cervical cancer offers an alternative approach when access to MRI restricts implementation of MRI. © 2014 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.
Advantages of a CBCT in Brachy Suite

- Intra-operative imaging
- Large mechanical clearance (scan in stirrups, make adjustments)
- Can be easily combined with other imaging modalities
- Minimize applicator/needles motion
- Ability to image and verify before treatment
- Can scan, plan and treat under anesthesia

How to set meaningful clinical flows?

- Understand CBCT limitations
- Initially compare CBCT contours for OARs with other imaging modalities (CT, MRI)
- Compare dose metrics ($D_{2cm}$) for OARs between planning image and pre-TX image
  - CBCT volumes vs. CBCT volumes
  - MRI volumes vs. CBCT volumes
- > 75 fractions analyzed

Good
2) Different cont MRI and pre-TX CBCT

![Images of MRI and CBCT scans]

**Actual changes in contours**

**What have we learned?**

- Anatomical variations in OAR between planning and Pre-TX (3-4 hrs. later) can be large so imaging before TX is recommended
- Pre treatment KV-CBCTs can be used as a check of the applicator positioning
- Potential large variations between MRI and CBCT planning contours
  - Attention for when CBCT is used alone
- In some cases, the KV-CBCT can identify a true change in anatomy that might confer more realistic dose metrics for dose summation purposes.
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What has access to MRI given us?

- Ability to clearly identify the target
- Realization that existent applicators are not optimal to cover the extent of the disease (intracavitary approach only)

What has access to MRI given us?

- GTVs > CTV
- Ambitious planning aims and dose-volume constraints
- New ICRU techniques
Vienna-style // Elekta and Varian

Components for Vienna-style Ring Applicator
- Compatible with compatibility combined instrument for greenstone & related endocytology of the stoma, lumen, and some stented
- Add-on for M beginner and high 2007 edition of the radiolung

Utrecht-style // Elekta

- ICIS approach
- Hybrid between ring and ovoids

Venezia // Elekta

- ICIS approach
- Hybrid between ring and ovoids
Free-hand Interstitial Needles

Intracavitary and custom bent free-hand interstitial needles is associated with reduced dose to the rectum, bladder and vagina.

Chen, Craciunescu et al., under review, 2016
EMBRACE II interventions

• Dose prescription (EBRT+BT):
  – Dose escalation in large tumours (HR-CTV vol > 40 cm³)
  – Dose de-escalation in small tumours (HR-CTV vol < 20 cm³)
  – OAR dose de-escalation as appropriate
  – Vaginal dose de-escalation in small and limited size tumors

• EBRT:
  – Application of IMRT + IGRT with reduced PTV margins (5 mm)
  – Application of risk adapted EBRT target volume
  – Focussed lymph node boosting

EMBRACE II dose prescription

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Started in 2009 under the guidance of Potter and Kirisits

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Reporting

Concepts and terminology for prescribing, recording, and reporting

In a level concept:

- **Level 1 - Minimum standard for reporting**
- **Level 2 - Advanced standard for reporting**
- **Level 3 - Research oriented reporting**

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Need for common terminology according to ICRU reports on proton treatment and IMRT

- **Planning aim dose**
  - A set of dose and volume constraints for a treatment

- **Prescribed dose**
  - A finally accepted treatment plan (which is assumed to be delivered to an individual patient)

- **Delivered dose**
  - Actually delivered dose to the individual patient

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Example:

- **Previously:** D97 dp = 84 Gy EQD2 prescribed; D99 was mean 99 Gy
- **Planning aim:** D97 dp = 84 Gy, D99 for rectum, sigmoid = 70 Gy EQD2, bladder = 90 Gy EQD2
- **Prescribed dose:** D90 dp = 13 Gy (100 Gy EQD2) to D9 HR-CTV
- **Delivered dose:** Depending on variations and uncertainties – an average on systematic deviations from prescribed dose

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Courtesy: C. Kirisits
Vaginal reference points

Conclusions: Role of Imaging in Modern Brachytherapy

• Unprecedented target visualization (MRI)
  – New guidelines for gynecological brachytherapy (ICRU 89)
    • Target delineation
    • Dose-volume metrics
  – New applicator design
• Design of new studies (Embrace II)
• Treatment response and prognosis via functional imaging

Thank you!
### Planning Aims

<table>
<thead>
<tr>
<th>Structure</th>
<th>D90 CTV&lt;sub&gt;HR&lt;/sub&gt; EQD2&lt;sub&gt;10&lt;/sub&gt;</th>
<th>D98 CTV&lt;sub&gt;HR&lt;/sub&gt; EQD2&lt;sub&gt;10&lt;/sub&gt;</th>
<th>D98 GTV EQD2&lt;sub&gt;10&lt;/sub&gt;</th>
<th>D98 CTV&lt;sub&gt;IR&lt;/sub&gt; EQD2&lt;sub&gt;10&lt;/sub&gt;</th>
<th>Point A EQD2&lt;sub&gt;10&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Planning Aims</td>
<td>&gt; 90 Gy &lt; 95 Gy</td>
<td>&gt; 75 Gy &lt; 95 Gy</td>
<td>&gt; 60 Gy</td>
<td>&gt; 60 Gy</td>
<td>&gt; 65 Gy</td>
</tr>
</tbody>
</table>

### Limits for Prescribed Dose

<table>
<thead>
<tr>
<th>Structure</th>
<th>Bladder D&lt;sub&gt;2cm³&lt;/sub&gt; EQD2&lt;sub&gt;3&lt;/sub&gt;</th>
<th>Rectum D&lt;sub&gt;2cm³&lt;/sub&gt; EQD2&lt;sub&gt;3&lt;/sub&gt;</th>
<th>Recto-vaginal point D&lt;sub&gt;2cm³&lt;/sub&gt; EQD2&lt;sub&gt;3&lt;/sub&gt;</th>
<th>Sigmoid/Bowel D&lt;sub&gt;2cm³&lt;/sub&gt; EQD2&lt;sub&gt;3&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Planning Aims</td>
<td>&lt; 80 Gy</td>
<td>&lt; 65 Gy</td>
<td>&lt; 70 Gy*</td>
<td>&lt; 70 Gy*</td>
</tr>
<tr>
<td>Limits for Prescribed Dose</td>
<td>&lt; 90 Gy</td>
<td>&lt; 75 Gy</td>
<td>&lt; 75 Gy*</td>
<td>&lt; 75 Gy*</td>
</tr>
</tbody>
</table>

* For the sigmoid/bowel structures, these dose constraints are valid in case of non-mobile bowel loops resulting in the situation that the most exposed volume is located at a similar part of the organ.

**EMBRACE II - dose prescription protocol**

**Planning Aims**

- Bladder D<sub>2cm³</sub> EQD2<sub>3</sub>
- Rectum D<sub>2cm³</sub> EQD2<sub>3</sub>
- Recto-vaginal point D<sub>2cm³</sub> EQD2<sub>3</sub>
- Sigmoid/Bowel D<sub>2cm³</sub> EQD2<sub>3</sub>

**Limits for Prescribed Dose**

- Bladder D<sub>2cm³</sub> EQD2<sub>3</sub>
- Rectum D<sub>2cm³</sub> EQD2<sub>3</sub>
- Recto-vaginal point D<sub>2cm³</sub> EQD2<sub>3</sub>
- Sigmoid/Bowel D<sub>2cm³</sub> EQD2<sub>3</sub>
Median volume = 32 cm³, 75 patients

Optimized with needles

Optimized without needles

Standard without needles
standard plan: prescribed dose to point A (left and right) no needles

\[ V_{pd} = 96 \text{ cm}^3 \]
\[ V_{2pd} = 29 \text{ cm}^3 \]

 COURTESY C. KIRISITS

optimized plan: prescribed dose to point A (right)

1 needle loaded

\[ V_{pd} = 103 \text{ cm}^3 \]
\[ V_{2pd} = 30 \text{ cm}^3 \]

 COURTESY C. KIRISITS

optimized plan: prescribed dose to point A (right)

2 needles loaded

\[ V_{pd} = 109 \text{ cm}^3 \]
\[ V_{2pd} = 33 \text{ cm}^3 \]

 COURTESY C. KIRISITS
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  - Functional imaging for response assessment
BOLD Imaging

Blood oxygen level-dependent (BOLD) imaging as a predictor of therapeutic response to concurrent chemoradiotherapy in cervical cancer: a preliminary experience

Jonathan H. Kim, Xiaojiang He, Carlos B. Azevedo, et al.

Table 2. T2* values of tumor and normal corpora, and the ratio of tumor vs. normal T2* values

<table>
<thead>
<tr>
<th>T2* Value</th>
<th>T2* Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal T2*</td>
<td>10.5 ± 1.2</td>
</tr>
<tr>
<td>Tumor T2*</td>
<td>16.0 ± 2.1</td>
</tr>
</tbody>
</table>

Data are the mean ± standard deviation (95% confidence interval) (n = 10 patients per group) month after the completion of treatment

MS-MRI: Improve visualization of target, OARs, applicators

Clinical implementation of multisequence MRI-based adaptive intracavitary brachytherapy for cervix cancer

Jacqueline E. Roberts, John Guerci-Farrell, Yehuda Ho, Samantha Stahl, Carol C. Schuhmann, Teresa Dy, Julie K. Schwann, and Gary W. Gralow

Journal of Clinical Oncology, Volume 27, Number 1, 2010

C. Treatment planning

T2W images, PDM images, and ADC maps were transferred to a treatment planning system by a medical physicist. Treatment planning was performed by a radiation oncologist using the TPS software. The treatment planning consisted of identifying the target volume, the dose distribution, and the OARs. The TPS software was used to simulate the treatment plan and to plan the dose distribution. The plan was then reviewed by the radiation oncologist and the patient's dose constraints were applied.
GTV contouring - T2W and ADC map

Plan Adaptation

Applicator Identification - PDW-MRI

Multisequence MRI technique: 1) improved visualization of the target volume, critical structures, and applicator.
2) Implementation of the dose tracking tools and dose adaptation technique by simply de-escalating Point A-based brachytherapy dose distributions will help balance target volume coverage with OAR sparing, without the need for more complex adaptation schemes.
MS-MRI: For TX response assessment using texture features

- For ADC maps calculated from DWM-MRI
- After CRT treatment, 22 out of 35 HR-CTV features significantly changed
- After HIF treatment (before 5th of HDR / before 1st of HDR), same 22 out of 35 HR-CTV features significantly changed
- For the whole treatment process, same 22 out of 35 HR-CTV features significantly changed

Texture features with significantly numerical changes can be used in monitoring radiotherapy effect in gynecological cancer
Texture features might be used as biomarkers which are supplementary to ADC for assessment of radiotherapy response in gynecological cancer