IMAGING FOR BRACHYTHERAPY PLANNING

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VOLUMES IN CARCINOMA CERVIX
# Rule of 15

<table>
<thead>
<tr>
<th>Stage</th>
<th>5 yr survival</th>
<th>%+ pelvic LN</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>II</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>III</td>
<td>55</td>
<td>45</td>
</tr>
</tbody>
</table>
II 50 Gy+ 10Gy

III

PROBABILITY OF TUMOR CONTROL
SUBCLINICAL:-45-50Gy
MICROSCOPIC:-50-60Gy
GROSS DISEASE:-80-85Gy
- 65-70 Gy
- 80-90 Gy
- 75-90 Gy
- 60-65 Gy
- < 45 Gy
- 120 Gy
Brachytherapy is Necessary

- Brachytherapy: internally delivered radiation using radioactive sources
- Supplements external beam
- Tumor control probability correlated with RT dose and cervix ca volume
  
  *Fletcher, J Radiol Electrol 56:383-400, 1975*

<table>
<thead>
<tr>
<th></th>
<th>External beam only</th>
<th>External Beam + brachytherapy</th>
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<tbody>
<tr>
<td><strong>4 yr Pelvic Control</strong></td>
<td>45%</td>
<td>67%</td>
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<tr>
<td></td>
<td>19%</td>
<td>46%</td>
</tr>
<tr>
<td><strong>4 yr Survival</strong></td>
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<tr>
<td><em>Lanciano JROBP 20:95, 1991</em></td>
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<tr>
<td><strong>Local Control</strong></td>
<td>40%</td>
<td>52%</td>
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<td><em>Montana Cancer 57:148, 1986</em></td>
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Brachytherapy Timeline

Technology

Discovery of Radioactivity
1896

1915: Radium Treatment

1970's: Caesium Treatments
Selectron LDR (afterloading)

1990's
Iridium-192 HDR/PDR

Present

Not formalised

Point based system

Volume based

Empirical prescription

1932: The Manchester dosage System (Point A introduced)

Dosimetric systems

3D Image guided, CT/MRI
Limitations – 2D imaging

POINT-A

• THEORETICAL REFERENCE POINT
• RELATES TO GENERIC ANATOMICAL POINT NOT INDIVIDUAL TUMOUR
• RELATIONSHIP WITH THE TUMOUR IS UNKNOWN
• VARIABLE DISTANCE TO TARGET AND OAR
• DOSE-EFFECT RELATIONSHIPS DIFFICULT TO ASSESS WITH POINT DOSES
  – POINT A WITH LOCAL CONTROL
  – ICRU BLADDER DOSE WITH BLADDER MORBIDITY
2D PLANNING

- LIMITATION OF POINT A DOSIMETRY
- INADEQUATE INFORMATION ABOUT TARGET VOLUME ASSESSMENT
- NO VOLUMETRIC INFORMATION ON ORGAN AT RISK

Where is the target volume (GTV? CTV?)

Where are the organs at risk?
The Problems

- ONE SIZE FITS ALL?
- UNDER TREAT LARGE TUMOURS
- OVER TREAT SMALL TUMOURS
Fallacies of ICRU Bladder Point
Tandem Ovoid Application
Fallacies of ICRU Bladder Point
Function of Bladder Filling

True B Max lies 1.5-3 cm cranial and lateral to ICRU point. B Max is often 2-3 times higher than ICRU point dose.
2D ICRU Point vs 3D CT based dosimetry

On comparing 2D with 3D, doses of OARs differed by 4-12%. Rectal doses are 1-1.6 times than 2D Planning and bladder doses 1.4-2.2 times.

ICRU Rectal point dose best correlated with 2 cc volume

ICRU Bladder Point Dose correlated with 13 cc volume. Gross Underreporting of Bladder doses.

Pelloski IJROBP 2005
Comparison between CT-based volumetric calculations and ICRU reference-point estimates of radiation doses delivered to bladder and rectum during intracavitary radiotherapy for cervical cancer

Christopher E. Pelloski, Matthew Palmer, B.S., Gregory M. Chronowski, Anuja Jhingran, John Horton, Patricia J. Eifel,

- Compared CT-based volumetric calculations and ICRU reference-point estimates of radiation doses to the bladder and rectum in patients with carcinoma cervix treated with definitive low-dose-rate intracavitary radiotherapy
- The minimal doses delivered to the 2 cm$^3$ of bladder and rectum receiving the highest dose ($D_{BV2}$ and $D_{RV2}$, respectively) were determined from dose-volume histograms, and these estimates were compared with two-dimensionally derived estimates of the doses to the corresponding ICRU reference points.

- **CONCLUSION**: ICRU rectal point may be a reasonable surrogate for the $D_{RV2}$
  - In contrast, the dose to the ICRU bladder point does not appear to be a reasonable surrogate for the $D_{BV2}$. 
RECENT IMAGING
MRI, CT, USG, PET

NEWER APPLICATORS

DEV IN TREATMENT
PLANNING SYSTEM

2D

VOLUME
BASED

Where is the target volume (GTV? CTV?)

Where are the organs at risk?
WHY IMAGING
## Imaging Procedures for Delineation of the GTV, CTV, PTV for Different Sites of Brachytherapy

<table>
<thead>
<tr>
<th>SITE</th>
<th>1ST CHOICE</th>
<th>2ND CHOICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobile Tongue</td>
<td>MRI</td>
<td>CT</td>
</tr>
<tr>
<td>Buccal Mucosa</td>
<td>MRI, CT, US</td>
<td></td>
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<tr>
<td>Oropharynx</td>
<td>MRI, ES</td>
<td>CT</td>
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<tr>
<td>Nasopharynx</td>
<td>ES, MRI</td>
<td>CT</td>
</tr>
<tr>
<td>Cervix</td>
<td>MRI</td>
<td>CT, US (ENDO)</td>
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<tr>
<td>Endometrium</td>
<td>MRI</td>
<td>ES, CT, US (ENDO)</td>
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<td>Mammography, MRI</td>
<td>CT, US</td>
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<tr>
<td>Bladder</td>
<td>ES, MRI, CT</td>
<td>US</td>
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<td>Prostate</td>
<td>MRI</td>
<td>US (ENDO), CT</td>
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<td>CT</td>
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<tr>
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<td>ES, Esophagogram, MRI</td>
<td>CT, MRI, US (ENDO)</td>
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<td>Cholangiogram, ES</td>
<td>CT, US, MRI</td>
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<td>MRI</td>
<td>CT</td>
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<td>MRI</td>
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<tr>
<td>Brain</td>
<td>MRI</td>
<td>CT</td>
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CARCINOMA CERVIX
WHY IMAGE ASSISTED?

- TUMOR REGRESSION
- ORGAN MOTION
- INTER AND INTRA FRACTION VARIATION
- TARGET VOLUME LOCALIZATION
- CONTOURING
- APPLICATOR RECONSTRUCTION
WHY IMAGING IN BRACHYTHERAPY CARCINOMA CERVIX

- DIAGNOSTIC IMAGING
- LOCALISATION IMAGING WITH APPLICATOR IN PLACE
- DELINEATION OF GTV, HR/IR CTV AND
- DOSE VOLUME PARAMETERS
IMAGING

IMAGE ASSISTED TREATMENT

- IMAGING AFTER APPLICATION FOR DEFINITIVE TREATMENT PLANNING (CR, US, CT, MRI) TO DERIVING TUMOR, ORGAN AT RISK, GTV, HIGH RISK CTV, INT RISK CTV

IMAGE GUIDED APPLICATION

IMAGED GUIDED APPLICATION, THE APPLICATION IS DONE UNDER GUIDANCE OF AN IMAGE PROCEDURE.

CR, MRI, CT, US, ES
3D DELINEATION OF THE PTV, INDICATING WIDTH, LENGTH AND THICKNESS AND AS FAR AS POSSIBLE THE TOPOGRAPHY RELATED TO SURROUNDING STRUCTURES.

“INTERNAL” TOPOGRAPHY OF THE TUMOUR

“EXTERNAL” POSITIONING OF THE PATIENT IS NOT AS IMPORTANT AS IN EXTERNAL BEAM THERAPY

ORGANS AT RISK IS CRUCIAL
SOME DEFINATION

CTV coverage: evaluated using V100, D90
• D90: Dose covering 90% of the volume
• V100: Volume that receives the prescribed dose
• High dose volume in CTV was estimated using V200.

For organs at risk (OARs): D0.1cc, D1cc, and D2cc
(i.e., minimum dose received by 0.1-, 1-, and 2-cm3 tissue volume) were calculated.

• GTVD, CTVD: Dose received at the time of external beam radiotherapy
• GTVB, CTVB: Dose received at the time of brachytherapy
Assessed DVH parameters for

- **Tumour**
  - GTV, HR CTV, IR CTV, D90, D100

- **Organs at risk**
  - Minimum dose in the most irradiated volume
  - D0.1cc, D1cc, D2cc

- **Express dose in EQD2 (Gy)**
  - Total dose (EBRT and BT) calculated with time and half life corrections in 2Gy equivalent ($\alpha/\beta$ ratio=10 target, $\alpha/\beta$ ratio=3 OAR)

*Potter et al. Radiother Oncol 2006;78:67*
Express dose in EQD2 (Gy)

- Total dose (EBRT and BT) calculated with time and half life corrections in 2Gy equivalent ($\alpha/\beta$ ratio=10 target, $\alpha/\beta$ ratio=3 OAR)

\[
\text{EQD}_{2_{\text{total}}} = \text{EQD}_{2_{\text{EBRT}}} + \text{EQD}_{2_{\text{ICR}}}
\]

\[
= Nd \left( \frac{(d + \alpha/\beta)}{(2 + \alpha/\beta)} \right) + N_B d_B \left[ \frac{(d_B + \alpha/\beta)}{(2 + \alpha/\beta)} \right]
\]

**Biologically Equivalent Dose**

Equivalent Dose in 2 Gy Fractions (EQD2)

\[
\text{BED} = nd(1+d/\alpha/\beta)/(1+2/\alpha/\beta)
\]

\[
\text{EQD2} = \text{BED}/1.2
\]

- $n$ = # fractions
- $d$ = dose/fraction
- $\alpha/\beta$ for tumor $\sim 10$
- $\alpha/\beta$ for normal tissue $\sim 3$

**Example:**

(5 fractions) x (5.5 Gy) x (1+5.5 Gy/10) / 1.2 = 35.5 Gy_{10}
IMAGING MODALITIES

• ULTRASOUND,
• COMPUTED TOMOGRAPHY,
• MAGNETIC RESONANCE
• PET CT SCAN
CT SCAN IN BRACHYTHERAPY

• WIDELY ACCEPTIBLE DUE TO EASILY ACCESSIBLE
• BLADDER, RECTUM WELL VISUALIZED
• METAL ARTIFACT
• POOR DIFFERENTIATION BETWEEN UTERUS, CERVIX, TUMOR, PARACERVICAL AREA
CT SCAN IN INTERSTITIAL IMPLANT

- Dosimetry
- Dose: 3.4 – 4 Gy /fraction
- 2 fractions per day 6 hours apart
- No of fractions: 4-6 depending on the response
Conformal Brachytherapy Planning for Cervical Cancer Using Transabdominal Ultrasound


- Seventy-one patients with locoregionally advanced cervix cancer were included.
- The protocol consisted of US-assisted tandem insertion and conformal US-based planning.
- Retrospectively, individual standard, US, and MRI plans were extrapolated for five fractions and superimposed onto the two-dimensional sagittal MRI images for comparison.
- US plan assessed on two-dimensional MRI image was comparable for target volume ($p = 0.11$), rectal point ($p = 0.8$), and vaginal mucosa ($p = 0.19$). Local control was 90%. Late bowel morbidity (G3, G4) was <2%.

Conclusions
Transabdominal ultrasound offers an accurate, quick, accessible, and cost-effective method of conformal brachytherapy planning.
MR BASED BRACHYTHERAPY

• MULTIPLANNAR IMAGE
• GOOD SOFT TISSUE CONTRAST
• DIFFERENTIATION BETWEEN UTERUS, CERVIX, TUMOR
• RECTUM, BLADDER, RECTOSIGMOID WELL VISUALISED
• SPECIAL MR COMPATIBLE APPLICATOR
• NOT AVAILABLE IN MANY CENTRES
(PARA)SAGITTAL (PARALLEL), PARACORONAL (PARALLEL) AND PARATRANSVERSE (90°) IMAGES (MRI) RELATED TO THE AXIS OF THE CERVIX CANAL AND THE UTERINE CAVITY IN UTERINE CANCER
## IMAGING PRINCIPLE

### CT IMAGES
- CT COMPATIBLE APPLICATORS
- IV AND RECTAL CONTRAST: TO BETTER OPACIFY THE BLADDER AND RECTOSIGMOID.
- IF ORAL CONTRAST: SCAN SHOULD BE PERFORMED 30 MINUTES AFTER ADMINISTRATION
- FOLEY CATHETER BULB SHOULD BE INFLATED WITH AIR
- SLICES THICKNESS: 3 MM OR LESS
- EXTEND OF SCAN: FROM AT LEAST 1 CM ABOVE THE TIP OF THE TANDEM TO THE BOTTOM OF THE ISCHIUM.

### MRI
- A NON-FERROMAGNETIC APPLICATOR
- T2 WEIGHTED MRI
- WHEN MOVING A PATIENT BETWEEN THE IMAGING UNIT AND THE TREATMENT ROOM: FIXATION OF THE APPLICATOR IS REQUIRED.
- INFUSE 50 CC OF WATER INTO THE BLADDER
- INFUSE 7 CC OF WATER IN FOLEY BULB
MRI IMAGES CA CERVIX

• Best possible imaging modality : MRI
• T2: hyperintense mass relative to normal stroma
• T1: isointense to normal stroma and may not be detectable
• T1: optimal sequence for assessment of lymphadenopathy.
• Fat saturation sequence can be used to differentiate between hemorrhage and fat
• With fat saturation techniques, fat appears dark (fat-saturated) and hemorrhage remains high in signal intensity.
Example images for comparison

- 2.5mm slice has more clearly defined boundaries due to reduction in partial volume effects
- Uterus typically curves out of image plane so edge boundary becomes more poorly defined with greater slice thickness
- Applicator demonstrates more partial volume in 4mm slice
• FAST SPIN ECHO (FSE): REDUCE MOTION ARTIFACT
• GADOLINIUM IS ROUTINELY USED IN THE EVALUATION OF ENDOMETRIAL AND OVARIAN DISEASE.
• GADOLINIUM IS NOT ROUTINELY USED IN THE STAGING OF CERVICAL CANCER AS IT HAS NOT BEEN SHOWN TO IMPROVE OVERALL STAGING ACCURACY

HELP DIFFERENTIATE VIABLE TUMOR FROM DEBRIS AND AREAS OF NECROSIS, AND ASSESS FOR BLADDER OR RECTAL INVOLVEMENT.
Inter and Intra fraction movement

- Fundus of uterus – max documented movement 48mm AP
- Uterus changes from anteverted to retroverted in 11%
- Cervix movement recorded
  - AP 2.3-16mm
  - Sup-inf 2.7-8mm
  - Lat 0.3-10mm
- Nodal movement – 5-9mm
- Intrafraction movement
  - cervix 0.1-3mm
  - >5mm in <5% of the time
  - Less with VMAT and Rapid Arc techniques

Tip of the fundus movement/bladder full vs empty

Jadon et al. Clin Oncol 2014:26;185
MRI PROCEDURES

• MRI:-1.5 TESLA MAGNET
• BOWEL MOTION :-FAST FOR 4-6 HOURS
• BUSCOPAN 20 MG IV OR IM JUST BEFORE THE EXAMINATION.
• THE AREA OF COVERAGE:-AORTIC BIFURCATION DOWN THROUGH THE INTROITUS WITH 24-28 CM FIELD OF VIEW
• 5MM SLICE THICKNESS WITH 1 MM GAP, 16 KHZ BANDWIDTH, 256-521 X 256 MATRIX AND NEX OF 2. AN ECHO TRAIN LENGTH (ETL) OF 8 WILL BE USED FOR THE FSE T2 SEQUENCES.
MRI SEQUENCE

- LOCALIZER, SAGITTAL PLANE
- SAGITTAL PLANE OF SECTION, FSE T2-WEIGHTED IMAGE.
- AXIAL PLANE OF SECTION, FSE T2-WEIGHTED IMAGE.
- AXIAL PLANE OF SECTION, T1-WEIGHTED IMAGE; SCAN TO RENAL HILUM IF PELVIC LYMPHADENOPATHY PRESENT.
- ONLY IF CANCER EXTENSION TO THE URINARY BLADDER OR RECTUM IS SUSPECTED AFTER REVIEWING THE NON-CONTRAST IMAGES, GADOLINIUM WILL BE ADMINISTERED AND A SAGITTAL PLANE OF SECTION, POSTCONTRAST T1 WILL BE OBTAINED.
- SEQUENCES REQUIRED FOR ASSESSING POSITION OF APPLICATOR: (B) AND (C) AS ABOVE WITH APPLICATOR IN PLACE. CAN USE SINGLE SHOT FSE T2, IF ADEQUATE.
### INFORMATION TO BE GATHERED FROM MRI

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TUMOR WIDTH, HEIGHT, THICKNESS</td>
<td>Information on tumor size and thickness.</td>
</tr>
<tr>
<td>BOTH THE PARAMETRIUM</td>
<td>Information on parametrium status.</td>
</tr>
<tr>
<td>TYPE OF INFILTRATION</td>
<td>Information on tumor infiltration type.</td>
</tr>
<tr>
<td>UTERUS, VAGINA</td>
<td>Information on the uterine and vaginal structures.</td>
</tr>
<tr>
<td>VAGINA ANT WALL</td>
<td>Information on anterior vaginal wall involvement.</td>
</tr>
<tr>
<td>VAGINA POST WALL</td>
<td>Information on posterior vaginal wall involvement.</td>
</tr>
<tr>
<td>PARAMETRIAL INV</td>
<td>Information on parametrial involvement.</td>
</tr>
<tr>
<td>VAGINAL EXTENSION</td>
<td>Information on vaginal extension.</td>
</tr>
<tr>
<td>BLADDER EXTENSION</td>
<td>Information on bladder extension.</td>
</tr>
<tr>
<td>RECTUM INVOLVEMENT</td>
<td>Information on rectal involvement.</td>
</tr>
</tbody>
</table>
APPLICATORS VS IMAGING

VISIBILITY, RELIABILITY, REPRODUCIBILITY OF THE APPLICATOR

IMAGE QUALITY OF THE TUMOUR AND THE ORGANS AT RISK

- ULTRASOUND BY ECHOGENIC NEEDLE TIPS (FOR EXAMPLE FOR PROSTATE)
- CT BY APPLICATORS NOT PRODUCING METALLIC ARTIFACTS
- MRI BY NON-METALLIC APPLICATORS AND NEEDLES
  - (FOR EXAMPLE FOR GYNAECOLOGY)
TARGET VOLUME DELINEATION
Target volume delineation
GTV D Vs GTV B

GTV D

GTV BT

HR CTV
IR CTV

GTV

High signal mass on T2 FSE images + clinical examination

High signal intensity mass on T2 FSE at the time of BT + examination
HRCTV:

- Extent of GTV at the time of BRACHY
- Whole Cervix
- Presumed Tumor
- Residual Grey Zone on MRI
- Gray Zone: Pathological Residual Disease as defined by palpable induration

IRCTV:

- Extent of GTV at the time of Diagnosis
- HRCTV
- Safety Margin
  - Cranial: -1 to 1.5 cm
  - Ant-Post: -.5 cm
  - Lateral: - 1 cm
NO PTV

GTV
Bladder

HRCTV
Rectum

IRCTV
Sigmoid

Bowel
Brachy better than IMRT

**Brachytherapy**
Moves with patient

**IMRT**
Does not move with patient
Difficult to adjust with response
OAR DELINEATION

- **BLADDER**: contour organ as outer wall. Prior to imaging empty bladder and instill 50 cc of saline.
- **RECTUM/BLADDER**: contour organ as outer wall.
- **SIGMOID**: recto sigmoid flexure and ends where sigmoid dislodges >2 cm from uterus/parametrium.
- **VAGINA**: gauze impregnated with 1:10 gadolinium or water based jelly and contour walls. 4 mm thickness.
CT versus MR contouring


- Width of contoured tumor larger on MRI
- OAR differences depend on filling status
- Nodal dose may be estimated
- Point A constant
OAR Delineation: Technique
Choice of Imaging Modality: CT vs MRI

Slight over-contouring on CT as compared to MRI. No difference in OAR doses. Either could be used for Dose Volume reporting for OARs

Vishwanathan IJROBP 2012
Krishnatry, Patel JJCO,
# GEC ESTRO: Dose Documentation

## Physical - Biological Documentation of Gynaecological HDR BT

<table>
<thead>
<tr>
<th>Patient ID-number</th>
<th>tumour entity</th>
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<tr>
<td>mum001</td>
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### External Beam Therapy

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<th>dose per fraction</th>
<th>TUMOUR</th>
<th>OAR</th>
<th>FIGO, TNM</th>
<th>IIB</th>
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<tbody>
<tr>
<td>dose per fraction</td>
<td>2</td>
<td>D&lt;sub&gt;iso&lt;/sub&gt; [α/β=10Gy]</td>
<td>D&lt;sub&gt;iso&lt;/sub&gt; [α/β=3Gy]</td>
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<tr>
<td>without central shield</td>
<td>20</td>
<td>40.0</td>
<td>40.0</td>
<td>GTV at diag.</td>
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<tr>
<td>total dose</td>
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### Brachytherapy

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<th>date</th>
<th>F 1</th>
<th>F 2</th>
<th>F 3</th>
<th>F 4</th>
<th>F 5</th>
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<td>svj</td>
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<td>TOTAL BT</td>
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<td>MR</td>
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<td>TOTAL BT + EBT</td>
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<tr>
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<td>VIENNA</td>
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<td>eval plan, remarks</td>
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### TRAK [cGy at 1m]

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<tr>
<th>prescribed dose PD</th>
<th>PD&lt;sub&gt;iso&lt;/sub&gt; [α/β=10Gy]</th>
<th>volume of PD [cm³]</th>
<th>PDx2</th>
<th>PDx2&lt;sub&gt;iso&lt;/sub&gt; [α/β=10Gy]</th>
<th>volume of PDx2 [cm³]</th>
<th>pres. point level (A / My / [mm])</th>
<th>pres. point (mm left / mm right)</th>
<th>dose to + A left</th>
<th>A&lt;sub&gt;left&lt;/sub&gt; - D&lt;sub&gt;iso&lt;/sub&gt; [α/β=10Gy]</th>
<th>dose to - A right</th>
<th>A&lt;sub&gt;right&lt;/sub&gt; - D&lt;sub&gt;iso&lt;/sub&gt; [α/β=10Gy]</th>
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PLANNING BRACHYTHERAPY

• EXAMINATION UNDER ANAESTHESIA
• PROPER APPLICATOR PLACEMENT
• MR IMAGING :-
  – T2 FSE,T1,SAG,AXIAL,CORONAL,CONTRAST
• CONTOURING:-
  – TUMOR:-GTV,HIGH RISK CTV,INTERMEDIATE RISK CTV
  – OAR:-D0.1CC,D-1CC,D-2CC
• TREATMENT PLANNING SYSTEM
  – CATHETER RECONSTRUCTION,
  – LOADING PATTERN,
  – OPTIMISATION
• PLAN EVALUATION:-
  – EQD2,DOSE TO GTV,HR CTV(D90,D100,V100)
  – DOSES TO OAR:- BLadder,RECTUM,SIGMOD(D0.1CC,D-1CC,D-2CC)
IS IT REALLY NECESSARY
CLINICAL IMPACT OF MRI ASSISTED DOSE VOLUME ADAPTATION AND DOSE ESCALATION IN BRACHYTHERAPY OF LOCALLY ADVANCED CERVIX CANCER.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>D90</td>
<td>81 GY</td>
<td>90 GY</td>
<td></td>
</tr>
<tr>
<td>OVERALL SURVIVAL</td>
<td>53%</td>
<td>64%</td>
<td>0.03</td>
</tr>
<tr>
<td>CSS</td>
<td>71%</td>
<td>90%</td>
<td>0.13</td>
</tr>
<tr>
<td>&gt;5 CM LOCAL CONTROL</td>
<td>64%</td>
<td>82%</td>
<td>0.09</td>
</tr>
<tr>
<td>OS</td>
<td>28%</td>
<td>58%</td>
<td>0.003</td>
</tr>
<tr>
<td>CSS</td>
<td>40%</td>
<td>62%</td>
<td>0.07</td>
</tr>
<tr>
<td>LATE MORBIDITY</td>
<td>10%</td>
<td>2%</td>
<td></td>
</tr>
</tbody>
</table>

Potter et al. Radiother Oncol 2007:83;148
MR T/R Brachytherapy Outcomes

- 156 patients
- Historical comparison
- Med FU 42 mo
- CR 97%
- Significant ↑
  - 3y OS 53 to 68%
  - CSS 62 to 74%
  - Tumors > 5cm
    - OS 28 to 65%

Local control 19 events: 96%
Cancer specific survival 43 events: 66%
Overall survival 59 events: 56%

Potter et al. Rad Oncol 2007
DOSE–VOLUME HISTOGRAM PARAMETERS AND LOCAL TUMOR CONTROL IN MAGNETIC RESONANCE IMAGE–GUIDED CERVICAL CANCER BRACHYTHERAPY

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*Department of Radiotherapy, Medical University of Vienna, Vienna, Austria; and †Department of Radiotherapy and Radiation Oncology, Medical Faculty Carl Gustav Carus, University of Technology, Dresden, Germany

Purpose: To investigate the value of dose–volume histogram (DVH) parameters for predicting local control in magnetic resonance (MR) image-guided brachytherapy (IGBT) for patients with cervical cancer.

Methods and Materials: Our study population consists of 141 patients with cervical cancer (Stages IB–IVA) treated with 45–50 Gy external beam radiotherapy plus four times 7 Gy IGBT with or without cisplatin. Gross tumor volume (GTV), high-risk clinical target volume (HRCTV), and intermediate-risk clinical target volume (IRCTV) were contoured, and DVH parameters (minimum dose delivered to 90% of the volume of interest [D90] and D100) were assessed. Doses were converted to the equivalent dose in 2 Gy (EQD2) by applying the linear quadratic model (α/β = 10 Gy). Groups were defined for patients with or without local recurrence (LR) in the true pelvis for tumor size at diagnosis (GTV at diagnosis [GTVD]) of 2–5 cm (Group 1) or greater than 5 cm (Group 2) and for tumor size response at IGBT (HRCTV) of 2–5 cm (Group 2a) or greater than 5 cm (Group 2b).

Results: Eighteen LRs were observed. The most important DVH parameters correlated with LR were the D90 and D100 for HRCTV. Mean D90 and D100 values for HRCTV were 86 ± 16 and 65 ± 10 Gy, respectively. The D90 for HRCTV greater than 87 Gy resulted in an LR incidence of 4% (3 of 68) compared with 20% (15 of 73) for D90 less than 87 Gy. The effect was most pronounced in the tumor group (Group 2b).

Conclusions: We showed an increase in local control in IGBT in patients with cervical cancer with the dose delivered, which can be expressed by the D90 and D100 for HRCTV. Local control rates greater than 95% can be achieved if the D90 (EQD2) for HRCTV is 87 Gy or greater. © 2009 Elsevier Inc.

Cervical cancer, Magnetic resonance (MR) image-guided brachytherapy, Target, Dose–volume histogram (DVH).
Table 4. D90 and D100 of three target structures for patients with/without LR and tumor size/response Groups 1, 2, 2a, and 2b

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>GTV</th>
<th>HR CTV</th>
<th>IR CTV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>D100 (Gy)</td>
<td>D90 (Gy)</td>
</tr>
<tr>
<td>1; 2–5cmDIAG</td>
<td>65</td>
<td>95 ± 27</td>
<td>131 ± 39</td>
</tr>
<tr>
<td>LR</td>
<td>2</td>
<td>92 ± 13</td>
<td>124 ± 19</td>
</tr>
<tr>
<td>No LR</td>
<td>63</td>
<td>95 ± 27</td>
<td>131 ± 39</td>
</tr>
<tr>
<td>p</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>2; &gt;5cmDIAG</td>
<td>76</td>
<td>86 ± 19</td>
<td>116 ± 29</td>
</tr>
<tr>
<td>LR</td>
<td>16</td>
<td>80 ± 12</td>
<td>111 ± 24</td>
</tr>
<tr>
<td>No LR</td>
<td>60</td>
<td>87 ± 20</td>
<td>117 ± 31</td>
</tr>
<tr>
<td>p</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>2a; &gt;5cmDIAG • 2–5cmBT</td>
<td>45</td>
<td>90 ± 21</td>
<td>122 ± 32</td>
</tr>
<tr>
<td>LR</td>
<td>5</td>
<td>90 ± 15</td>
<td>134 ± 29</td>
</tr>
<tr>
<td>No LR</td>
<td>40</td>
<td>90 ± 22</td>
<td>121 ± 33</td>
</tr>
<tr>
<td>p</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>2b; &gt;5 cmDIAG • &gt;5 cmBT</td>
<td>31</td>
<td>79 ± 14</td>
<td>106 ± 22</td>
</tr>
<tr>
<td>LR</td>
<td>11</td>
<td>76 ± 9</td>
<td>101 ± 12</td>
</tr>
<tr>
<td>No LR</td>
<td>20</td>
<td>81 ± 17</td>
<td>109 ± 25</td>
</tr>
<tr>
<td>p</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

**Abbreviations:** GTV = gross tumor volume; CTV = clinical target volume; HR = high risk; IR = intermediate risk; Dx = minimum dose delivered to x% of the volume of interest; LR = local recurrence; 2–5cmDIAG = tumors 2–5 cm at diagnosis; >5cmDIAG = tumors greater than 5 cm at diagnosis; >5cmDIAG • 2–5cmBT = tumors greater than 5 cm at diagnosis and HRCTV of 2–5cm at the time of brachytherapy; >5 cmDIAG • >5 cmBT = tumors greater than 5 cm at diagnosis and HRCTV greater than 5 cm at the time of brachytherapy.

Dose values expressed as mean ± 1 SD equivalent doses for 2 Gy fractions (EQD2; α/β = 10 Gy).

Bold values indicate significant p values.
Reference tolerance doses

• For D2cc (Gy)
  – Rectum, bowel, sigmoid – 75Gy
  – Bladder – 95Gy
DVH analysis and late side effects

• Rectum: D2cc rectum >75 Gy predicted > G2 side effects

• Sigmoid: No dose limit identified given low number of sigmoid specific side effects

• Bladder: D2cc >95 Gy appeared to increase side effects though further analysis needed
## Dose effect relationship for late side effects and IGABT - Rectum

- Probability of EQD2 for G2-4 side effects (Gy) for the incidence rates shown (95% CI)

<table>
<thead>
<tr>
<th>Dose volume</th>
<th>5%</th>
<th>10%</th>
<th>20%</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2cc</td>
<td>67 (30-79)</td>
<td>78 (66-110)</td>
<td>90 (78-171)</td>
<td>0.0178</td>
</tr>
<tr>
<td>D1cc</td>
<td>71 (0-89)</td>
<td>87 (69-209)</td>
<td>104 (87-443)</td>
<td>0.0352</td>
</tr>
<tr>
<td>D0.1cc</td>
<td>83</td>
<td>132</td>
<td>186</td>
<td>0.1364</td>
</tr>
</tbody>
</table>

Georg et al. IJROBP 2012;82(2):653
Dose effect relationship for late side effects and IGABT - Bladder

- Probability of EQD2 for G2-4 side effects (Gy) for the incidence rates shown (95% CI)

<table>
<thead>
<tr>
<th>Dose volume</th>
<th>5% (95% CI)</th>
<th>10% (95% CI)</th>
<th>20% (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2cc</td>
<td>70 (0-95)</td>
<td>101 (29-137)</td>
<td>134 (110-371)</td>
<td>0.0274</td>
</tr>
<tr>
<td>D1cc</td>
<td>71 (0-107)</td>
<td>116 (17-169)</td>
<td>164 (129-498)</td>
<td>0.0268</td>
</tr>
<tr>
<td>D0.1cc</td>
<td>61 (0-155)</td>
<td>178 (0-368)</td>
<td>305 (129-498)</td>
<td>0.0369</td>
</tr>
</tbody>
</table>

Georg et al. IJROBP 2012;82(2):653
Table 1. Dose levels (in grays) and side effects (Group 1 vs. Group 2) for the rectum, sigmoid colon, and urinary bladder

<table>
<thead>
<tr>
<th>OAR</th>
<th>n</th>
<th>$D_{icru}$</th>
<th>$D_{2cc}$</th>
<th>$D_{1cc}$</th>
<th>$D_{0.1cc}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>141</td>
<td>72 ± 15</td>
<td>95 ± 22</td>
<td>108 ± 31</td>
<td>162 ± 75</td>
</tr>
<tr>
<td>Group 1 (G0)</td>
<td>118</td>
<td>71 ± 15</td>
<td>94 ± 20</td>
<td>107 ± 28</td>
<td>158 ± 65</td>
</tr>
<tr>
<td>Group 2 (G1–G4)</td>
<td>23</td>
<td>76 ± 16</td>
<td>101 ± 29</td>
<td>117 ± 42</td>
<td>182 ± 116</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.144</td>
<td>0.197</td>
<td>0.159</td>
<td>0.168</td>
</tr>
<tr>
<td>Rectum</td>
<td>141</td>
<td>67 ± 13</td>
<td>65 ± 12</td>
<td>69 ± 14</td>
<td>86 ± 27</td>
</tr>
<tr>
<td>Group 1 (G0)</td>
<td>130</td>
<td>66 ± 12</td>
<td>64 ± 12</td>
<td>69 ± 14</td>
<td>84 ± 26</td>
</tr>
<tr>
<td>Group 2 (G1–G4)</td>
<td>11</td>
<td>80 ± 19</td>
<td>75 ± 13</td>
<td>80 ± 16</td>
<td>103 ± 31</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.002*</td>
<td>0.003*</td>
<td>0.007*</td>
<td>0.022*</td>
</tr>
<tr>
<td>Sigmoid</td>
<td>141</td>
<td>62 ± 12</td>
<td>67 ± 14</td>
<td>84 ± 32</td>
<td></td>
</tr>
<tr>
<td>Group 1 (G0)</td>
<td>138</td>
<td>62 ± 12</td>
<td>66 ± 14</td>
<td>83 ± 33</td>
<td></td>
</tr>
<tr>
<td>Group 2 (G1–G4)</td>
<td>3</td>
<td>77 ± 11</td>
<td>84 ± 14</td>
<td>104 ± 24</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.028*</td>
<td>0.037*</td>
<td>0.279</td>
<td></td>
</tr>
</tbody>
</table>

* Abbreviations: OAR = organ at risk; $D_{icru}$ = dose at the International Commission on Radiation Units and Measurements reference point; $D_{2cc}$, $D_{1cc}$, $D_{0.1cc}$ = most exposed 2, 1, and 0.1 cm$^3$ of tissue; G = Grade.

* Statistically significant ($p < 0.05$).
DOSE–VOLUME HISTOGRAM PARAMETERS AND LATE SIDE EFFECTS IN MAGNETIC RESONANCE IMAGE–GUIDED ADAPTIVE CERVICAL CANCER BRACHYTHERAPY


*Department of Radiotherapy, Medical University of Vienna, Vienna, Austria; and †Department of Radiotherapy and Radiation Oncology, Medical Faculty Carl Gustav Carus, University of Technology Dresden, Dresden, Germany

Table 2. Dose levels (in grays) and side effects (Group 3 vs. Group 4) for the rectum, sigmoid colon, and urinary bladder

<table>
<thead>
<tr>
<th>OAR</th>
<th>n</th>
<th>D_{IRCUN}</th>
<th>D2 cc</th>
<th>D1 cc</th>
<th>D0.1 cc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>141</td>
<td>72 ± 15</td>
<td>95 ± 22</td>
<td>108 ± 31</td>
<td>162 ± 75</td>
</tr>
<tr>
<td>Group 3 (G0–G1)</td>
<td>127</td>
<td>71 ± 15</td>
<td>94 ± 20</td>
<td>106 ± 28</td>
<td>157 ± 63</td>
</tr>
<tr>
<td>Group 4 (G2–G4)</td>
<td>14</td>
<td>78 ± 15</td>
<td>108 ± 33</td>
<td>126 ± 48</td>
<td>208 ± 140</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.133</td>
<td>0.021*</td>
<td>0.019*</td>
<td>0.016*</td>
</tr>
<tr>
<td>Rectum</td>
<td>141</td>
<td>67 ± 13</td>
<td>65 ± 12</td>
<td>69 ± 14</td>
<td>86 ± 27</td>
</tr>
<tr>
<td>Group 3 (G0–G1)</td>
<td>133</td>
<td>66 ± 12</td>
<td>64 ± 12</td>
<td>69 ± 14</td>
<td>85 ± 26</td>
</tr>
<tr>
<td>Group 4 (G2–G4)</td>
<td>8</td>
<td>83 ± 22</td>
<td>75 ± 15</td>
<td>80 ± 18</td>
<td>100 ± 30</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.001*</td>
<td>0.014*</td>
<td>0.030*</td>
<td>0.122</td>
</tr>
<tr>
<td>Sigmoid</td>
<td>141</td>
<td>62 ± 12</td>
<td>67 ± 14</td>
<td>84 ± 32</td>
<td></td>
</tr>
<tr>
<td>Group 3 (G0–G1)</td>
<td>138</td>
<td>62 ± 12</td>
<td>66 ± 14</td>
<td>83 ± 33</td>
<td></td>
</tr>
<tr>
<td>Group 4 (G2–G4)</td>
<td>3</td>
<td>77 ± 11</td>
<td>84 ± 14</td>
<td>104 ± 24</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.028*</td>
<td>0.037*</td>
<td>0.279</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.
* Statistically significant (p < 0.05).
Comparative Study of LDR (Manchester System) and HDR Image-guided Conformal Brachytherapy of Cervical Cancer: Patterns of Failure, Late Complications, and Survival


- Retrospective study of 217 patients of advanced carcinoma cervix.
- 90 patients received LDR and 123 patients received HDR brachytherapy
- **Conclusion** of the study-- Image-guided HDR planning led to a large decrease in late radiation effects in patients treated by HDR. Patterns of failure and survival were similar in patients treated either by LDR or HDR.
Tumor control related to dose


- D90 for HRCTV > 87 Gy
  - LR 4% (3 of 68)

- D90 for HRCTV ≤ 87 Gy
  - LR 20% (15 of 73)

- The effect was most pronounced in patients that had tumors >5cm with a poor response
TAKE HOME MESSAGE
IMAGE ASSISTED BRACHYTHERAPY

• BRACHY THERAPY IS AN INTEGRAL PART OF TREATMENT
• MRI IS THE BEST MODALITY OF IMAGING
• T2 FSE IMAGING TO DELINEATE THE TUMOR
• CONTOURING:-
  – TUMOR:-GTV, HIGH RISK CTV, INTERMEDIATE RISK CTV
  – OAR:-0.1CC, 1CC, 2CC
  – BETTER TUMOR CONTROL AND LESS MORBIDITY
Strategize your approach

- Experience matters
  - Training programs
- Follow guidelines
- Standardize approach

“I like to practice before I start acupuncture treatment!”