### IMAGING FOR BRACHYTHERAPY PLANNING

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### **VOLUMES IN CARCINOMA CERVIX**

PA.LN

RA,C.LN

Tiz

# Rule of 15

Stage	5 yr survival	%+ pelvic LN
Ι	85	15
II	70	30
III	55	45







#### **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

	External beam only	External Beam + brachytherapy
4 y Pelvic Control	45% 19%	<u>67</u> % <u>46</u> %
4 y Survival Lanciano JROBP 20:95, 1991		
Local Control Montana Cancer 57:148, 1986	40%	<u>52</u> %

# Brachytherapy Timeline

#### <u>Technology</u>



# 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





# The Problems

- ONE SIZE FITS ALL?
- UNDER TREAT LARG
   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

Watchner Gerstner R and O 2003

#### 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<sup>3</sup> 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  $\mathsf{D}_{\mathsf{RV2}}$ 
  - In contrast, the dose to the ICRU bladder point does not appear to be a reasonable surrogate for the  $D_{BV2}$ .



### WHY IMAGING



#### IMAGING PROCEDURES FOR DELINEATION OF THE GTV,CTV,PTV FOR DIFFERENT SITES OF BRACHYTHERAPY

SITE	1ST CHOICE	2ND CHOICE
MOBILE TONGUE	MRI	СТ
<b>BUCCAL MUCOSA</b>	MRI,CT, US	
OROPHARYNX	MRI,ES	СТ
NASOPHARYNX	ES, MRI	СТ
CERVIX	MRI	CT, US (ENDO)
ENDOMETRIUM	MRI	ES, CT, US (ENDO)
BREAST	MAMMOGRAPHY,MRI	CT, US
BLADDER	ES, MRI, CT	US
PROSTATE	MRI	US (ENDO), CT
ANORECTAL	ES, MRI, US (ENDO)	СТ
OESOPHAGUS	ES, ESOPHAGOGRAM	CT,MRI,US (ENDO)
BILE DUCT	CHOLANGIGRAM,ES	CT, US, MRI
SOFT TISSUE SARCOMA	MRI	СТ
BRONCHUS	ES,CT,CHEST X-RAY	MRI
BRAIN	MRI	СТ

# 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



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

#### (GYN) GEC ESTRO Working Group (II) 3D dose volume parameters

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 (α/β ratio=10 target, α/β 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 (α/β ratio=10 target, α/β ratio=3 OAR)

$$\begin{split} \mathrm{EQD2}_{\mathrm{total}} &= \mathrm{EQD}\, 2_{\mathrm{EBRT}} + \mathrm{EQD}\, 2_{\mathrm{ICR}} \\ &= \mathrm{Nd}\, [(\mathrm{d} + \alpha/\beta)/\left(2 + \alpha/\beta\right)] \\ &+ \mathrm{N_Bd_B}\, [(\mathrm{d_B} + \alpha/\beta)/\left(2 + \alpha/\beta\right)] \end{split}$$

#### Biologically Equivalent Dose Equivalent Dose in 2 Gy Fractions (EQD2) BED= nd(1+d/α/β)/(1+2/ α/β)

#### EQD2= BED/1.2

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

#### Example:

(5 fractions) x (5.5 Gy) x (1+5.5 Gy/10) / 1.2 = 35.5 Gy<sub>10</sub>

# 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





#### Conformal Brachytherapy Planning for Cervical Cancer Using Transabdominal Ultrasound

Sylvia Van Dyk, D.App.Sc. ,Kailash Narayan, Franzcr.,Richard Fisher,., David Bernshaw, Franzcr

- 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%.</li>

#### 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
- DIFFERNTIATION BETWEEN UTERUS,CERVIX,TUMOR
- RECTUM, BLADDER, RECTOSI GMOID 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 7CC 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

4mm (1mm gap)



2.5mm(2.5mm gap)



- 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

# CONTD.

- 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

IORADIATION VS RADIATION ALO

#### MRI PROCEDURES

# 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

TUMOR WIDTH, HEIGHT, THICKNES BOTH THE PARAMETRIUM TYPE OF INFILTRATION UTERUS, VAGINA VAGINA ANT WALL VAGINA POST WALL PARAMETRIAL IINV VAGINAL EXTESION **BLADDER EXTENSION RECTUM INVOLVEMENT** 



### **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**



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

- EXTENT OF GTV AT THE TIME OF DIAGNOSIS
- HRCTV
- SAFETY MARGIN
  - CRANIAL:-1 TO 1.5 CM
  - ANT-POST:-.5CM
  - LATERAL:- 1CM

# NO PTV



GTVHRCTVIRCTVBladderRectumSigmoidBowel

#### **Brachy better than IMRT**





#### 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**

Viswanathan et al. Int J Radiat Oncol Biol 2007;68(2):491-498.



- 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

	OARs	MRI	CT
	Bladder		
	Volume (cm <sup>3</sup> )	$62.5 \pm 31.6$	$84.5 \pm 57.5$
Bladder	$D_{0.1cm}^{3}$	$7.5 \pm 1.0$	$6.5 \pm 1.5$
	D <sub>1</sub> m <sup>3</sup>	$6.1 \pm 0.6$	$5.5 \pm 1.4$
	D <sub>2cm</sub> <sup>3</sup>	$5.6 \pm 0.6$	$5.0 \pm 1.2$
MR	Rectum		
	Volume (cc)	$45.3 \pm 15.3$	$62.8 \pm 16.8^*$
TO — CT	$D_{0.1cm}^{3}$	$5.0 \pm 0.9$	$5.0 \pm 1.1$
HR-CTV	Dicm	$4.2 \pm 0.7$	$4.2 \pm 0.9$
	D <sub>02cm</sub> <sup>3</sup>	$3.9 \pm 0.7$	$3.9 \pm 0.8$
Company and the second s	Sigmoid		
	Volume (cc)	$36.5 \pm 25.2$	$29.8 \pm 16$
	Do lom <sup>3</sup>	$5.5 \pm 1.1$	$5.5 \pm 1.9$
(recrum)	D13	$4.5 \pm 0.9$	$4.3 \pm 1.5$
	D <sub>2cm</sub> <sup>1cm</sup> <sub>3</sub>	$4.0 \pm 0.8$	$3.9 \pm 1.4$

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

_									
PA	TIENT, ID-number	mum001						tumour entity	
E)	TERNAL BEAM THERAF	γ		TUMOUR		OAR		FIGO, TNM	IIB
	dose per fraction	2		Dies [a/B=10Gv]		Dien [a/B=3Gv]			
	fractions without central shield	20		40.0		40.0			
	fractions with central shield	0		0.0		0.0		GTV at diag.	cm <sup>3</sup>
	total dose	40.0		40.0		40.0			
								chemoth.	WEEKLY
B	RACHYTHERAPY	F 1	F 2	F 3	F 4	F 5	F 6		
	date	23/8/11	30/8/11	7/9/11				dose	values in Gy
	physicist	svj	svj	svj	svj				
	MR / CT	MR	MR	MR	MR			TOTAL	TOTAL
	applicator(s): type	VIENNA	VIENNA					BT	BT + EBT
	applicator(s): dimensions	30/60MM	30/60MM						
	eval plan, remarks	1						mean	stddev
	TRAK [cGy at 1m]							0.00	
	prescribed dose PD	7	7	7	0	0			
	PD iso [α/β=10Gy]	9.9	9.9	9.9	0.0	0.0	0.0	29.8	69.8
	volume of PD [cm <sup>3</sup> ]							#DIV/0!	#DIV/0!
	PDx2	14.0	14.0	14.0	0.0	0.0	0.0		
	PDx2 <sub>iso</sub> [α/β=10Gy]	28.0	28.0	28.0	0.0	0.0	0.0	84.0	124.0
	volume of PDx2 [cm <sup>3</sup> ]							#DIV/0!	#DIV/0!
	pres. point level (A / My / [mm])								
	pres. point [mm left / mm right]								
	dose to + A left	7.0	7.0	7.0	0.0	0.0			
	A <sub>left</sub> - D <sub>iso</sub> [α/β=10Gy]	9.9	9.9	9.9	0.0	0.0	0.0	29.8	69.8
	dose to - A right	7.0	7.0	7.0	0.0	0.0			
	A <sub>right</sub> - D <sub>iso</sub> [α/β=10Gy]	9.9	9.9	9.9	0.0	0.0	0.0	29.8	69.8

# 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.

	CONV BRACHY 1998-2000	MRI BASED BRACHY 2001-2003	р
D90	81 GY	90 GY	
OVERALL SURVIVAL	53%	64%	0.03
CSS	71%	90%	0.13
>5 CM LOCAL CONTROL	64%	82%	0.09
OS	28%	58%	0.003
CSS	40%	62%	0.07
LATE MORBIDITY	10%	2%	

Potter et al. Radiother Oncol 2007:83;148

#### **MR T/R Brachytherapy Outcomes**

Rad Onc 2011:100:116-123

- 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%



Pötter et al. Rad Oncol 2007

#### DOSE-VOLUME HISTOGRAM PARAMETERS AND LOCAL TUMOR CONTROL IN MAGNETIC RESONANCE IMAGE-GUIDED CERVICAL CANCER BRACHYTHERAPY

JOHANNES C. A. DIMOPOULOS, M.D.,\* STEFAN LANG, PH.D.,\* CHRISTIAN KIRISITS, D.Sc.,\* ELENA F. FIDAROVA, M.D.,\* DANIEL BERGER, M.Sc.,\* PETRA GEORG, M.D.,\* WOLFGANG DÖRR, D.V.M., PH.D.,<sup>†</sup> AND RICHARD PÖTTER, M.D.\*

\*Department of Radiotherapy, Medical-University of Vienna, Vienna, Austria; and <sup>†</sup>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 ( $\alpha/\beta = 10$  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).

Cervical cancer DVH-parameters and local tumor control ● J. C. A. DIMOPOULOS et al.

		GTV		HR CTV		IR CTV	
Subgroup	n	D100 (Gy)	D90 (Gy)	D100 (Gy)	D90 (Gy)	D100 (Gy)	D90 (Gy)
1; 2-5cmDIAG	65	$95 \pm 27$	$131 \pm 39$	$65 \pm 11$	89 ± 17	$51 \pm 8$	$65 \pm 10$
LR	2	$92 \pm 13$	$124 \pm 19$	$69 \pm 1$	$92 \pm 3$	$53 \pm 1$	$69 \pm 1$
No LR	63	$95 \pm 27$	$131 \pm 39$	$65 \pm 12$	$89 \pm 17$	$51 \pm 8$	$65 \pm 10$
p		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
2; >5cmDIAG	76	$86 \pm 19$	$116 \pm 29$	$65 \pm 8$	$83 \pm 15$	$55 \pm 5$	$66 \pm 8$
LR	16	$80 \pm 12$	$111 \pm 24$	$59 \pm 6$	$73 \pm 11$	$53 \pm 5$	$61 \pm 6$
No LR	60	$87 \pm 20$	$117 \pm 31$	$66 \pm 8$	$86 \pm 15$	$56 \pm 4$	$67 \pm 8$
p		>0.05	>0.05	<0.05	<0.05	<0.05	<0.05
2a; >5cmDIAG • 2-5cmBT	45	$90 \pm 21$	$122 \pm 32$	$67 \pm 8$	88 ± 15	$56 \pm 4$	$68 \pm 7$
LR	5	$90 \pm 15$	$134 \pm 29$	$62 \pm 4$	83 ± 7	$52 \pm 7$	$64 \pm 4$
No LR	40	$90 \pm 22$	$121 \pm 33$	$68 \pm 8$	$88 \pm 15$	$56 \pm 4$	$68 \pm 7$
p		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
2b; >5 cmDIAG • >5 cmBT	31	$79 \pm 14$	$106 \pm 22$	$61 \pm 8$	$77 \pm 13$	$55 \pm 5$	$63 \pm 8$
LR	11	$76 \pm 9$	$101 \pm 12$	$57 \pm 7$	69 ± 9	$53 \pm 4$	$60 \pm 6$
No LR	20	$81 \pm 17$	$109 \pm 25$	$64 \pm 7$	$81 \pm 13$	$56 \pm 5$	$65 \pm 8$
<i>p</i>		>0.05	>0.05	<0.05	<0.05	>0.05	>0.05

Table 4. D90 and D100 of three target structures for patients with/without LR and tumor size/response Groups 1, 2, 2a, and 2b

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  $\pm 1$  SD equivalent doses for 2 Gy fractions (EQD2;  $\alpha/\beta = 10$  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**

Georg et al. Int J Radiat Oncol Biol Phys. 2011 Feb 1;79(2):356-62

- 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)

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

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)

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

Georg et al. IJROBP 2012;82(2):653



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#### **CLINICAL INVESTIGATION**

Cervix

#### DOSE-VOLUME HISTOGRAM PARAMETERS AND LATE SIDE EFFECTS IN MAGNETIC RESONANCE IMAGE-GUIDED ADAPTIVE CERVICAL CANCER BRACHYTHERAPY

PETRA GEORG, M.D.,\* STEFAN LANG, PH.D.,\* JOHANNES C. A. DIMOPOULOS, M.D.,\* WOLFGANG DÖRR, D.V.M., PH.D.,\*<sup>†</sup> ALINA E. STURDZA, M.D.,\* DANIEL BERGER, PH.D.,\* DIETMAR GEORG, PH.D.,\* CHRISTIAN KIRISITS, D.Sc.,\* AND RICHARD PÖTTER, M.D.\*

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OAR	n	DICRU	D <sub>2ce</sub>	D <sub>1cc</sub>	D <sub>0.1cc</sub>
Bladder	141	$72 \pm 15$	$95\pm22$	$108 \pm 31$	$162 \pm 75$
Group 1 (G0)	118	$71 \pm 15$	$94 \pm 20$	$107 \pm 28$	$158\pm65$
Group 2 (G1-G4)	23	$76 \pm 16$	$101 \pm 29$	$117 \pm 42$	$182 \pm 116$
p		0.144	0.197	0.159	0.168
Rectum	141	$67 \pm 13$	$65 \pm 12$	$69 \pm 14$	$86 \pm 27$
Group 1 (G0)	130	$66 \pm 12$	$64 \pm 12$	$69 \pm 14$	$84 \pm 26$
Group 2 (G1-G4)	11	$80 \pm 19$	$75 \pm 13$	$80 \pm 16$	$103 \pm 31$
p		0.002*	0.003*	0.007*	0.022*
Sigmoid	141		$62 \pm 12$	$67 \pm 14$	$84 \pm 32$
Group 1 (G0)	138		$62 \pm 12$	$66 \pm 14$	$83 \pm 33$
Group 2 (G1–G4)	3		$77 \pm 11$	$84 \pm 14$	$104 \pm 24$
<i>p</i>			0.028*	0.037*	0.279

Table 1. Dose levels (in grays) and side effects (Group 1 vs. Group 2) for the rectum, sigmoid colon, and urinary bladder

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<sup>3</sup> of tissue; G = Grade.

\* Statistically significant (p < 0.05).



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#### **CLINICAL INVESTIGATION**

Cervix

#### DOSE-VOLUME HISTOGRAM PARAMETERS AND LATE SIDE EFFECTS IN MAGNETIC RESONANCE IMAGE-GUIDED ADAPTIVE CERVICAL CANCER BRACHYTHERAPY

PETRA GEORG, M.D.,\* STEFAN LANG, PH.D.,\* JOHANNES C. A. DIMOPOULOS, M.D.,\* WOLFGANG DÖRR, D.V.M., PH.D.,\*<sup>†</sup> ALINA E. STURDZA, M.D.,\* DANIEL BERGER, PH.D.,\* DIETMAR GEORG, PH.D.,\* CHRISTIAN KIRISITS, D.Sc.,\* AND RICHARD PÖTTER, M.D.\*

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OAR	n	D <sub>ICRU</sub>	D2 cc	D1 cc	D0.1 cc
Bladder	141	$72 \pm 15$	$95 \pm 22$	$108 \pm 31$	$162 \pm 75$
Group 3 (G0-G1)	127	$71 \pm 15$	$94 \pm 20$	$106 \pm 28$	$157 \pm 63$
Group 4 (G2-G4)	14	$78 \pm 15$	$108 \pm 33$	$126 \pm 48$	$208 \pm 140$
p		0.133	0.021*	0.019*	0.016*
Rectum	141	$67 \pm 13$	$65 \pm 12$	$69 \pm 14$	$86 \pm 27$
Group 3 (G0-G1)	133	$66 \pm 12$	$64 \pm 12$	$69 \pm 14$	$85 \pm 26$
Group 4 (G2-G4)	8	$83 \pm 22$	$75 \pm 15$	$80 \pm 18$	$100 \pm 30$
p		0.001*	0.014*	0.030*	0.122
Sigmoid	141		$62 \pm 12$	$67 \pm 14$	$84 \pm 32$
Group 3 (G0-G1)	138		$62 \pm 12$	$66 \pm 14$	$83 \pm 33$
Group 4 (G2-G4)	3		$77 \pm 11$	$84 \pm 14$	$104 \pm 24$
р	00141		0.028*	0.037*	0.279

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

Abbreviations as in Table 1.

\* Statistically significant (p < 0.05).



#### Comparative Study of LDR (Manchester System) and HDR Imageguided Conformal Brachytherapy of Cervical Cancer: Patterns of Failure, Late Complications, and Survival

Kailash Narayan, F.R.A.N.Z.C.R.correspondenceemail, Sylvia van Dyk, Dip App Sci, David Bernshaw, F.R.A.N.Z.C.R., Chrishanthi Rajasooriyar, M.D. , Srinivas Kondalsamy-Chennakesavan,

- 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**

Dimopoulos JC et al. Int J Radiat Oncol Biol Phys. 2009 Sep 1;75(1):56-63

- D90 for HRCTV > 87 Gy
  - LR 4% (3 of 68)
- D90 for HRCTV < 87 Gy</li>
   LR 20% (15 of 73)
- The effect was most pronounced in patients that had tumors >5cm w 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

