

XXII CONGRESSO  
**AIRO**

**ROMA 2012**

17-20 novembre  
Ergife Palace Hotel



Associazione  
Italiana  
Radioterapia  
Oncologica



**TRATTAMENTI INTEGRATI NEL CARCINOMA DELLA VULVA**

***La Pianificazione e I Volumi di  
Trattamento***

**PAOLO MUTO**

**Direttore UOC Radioterapia**


**ISTITUTO NAZIONALE TUMORI IRCCS Fondazione Pascale di Napoli**

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# Ca Vulva

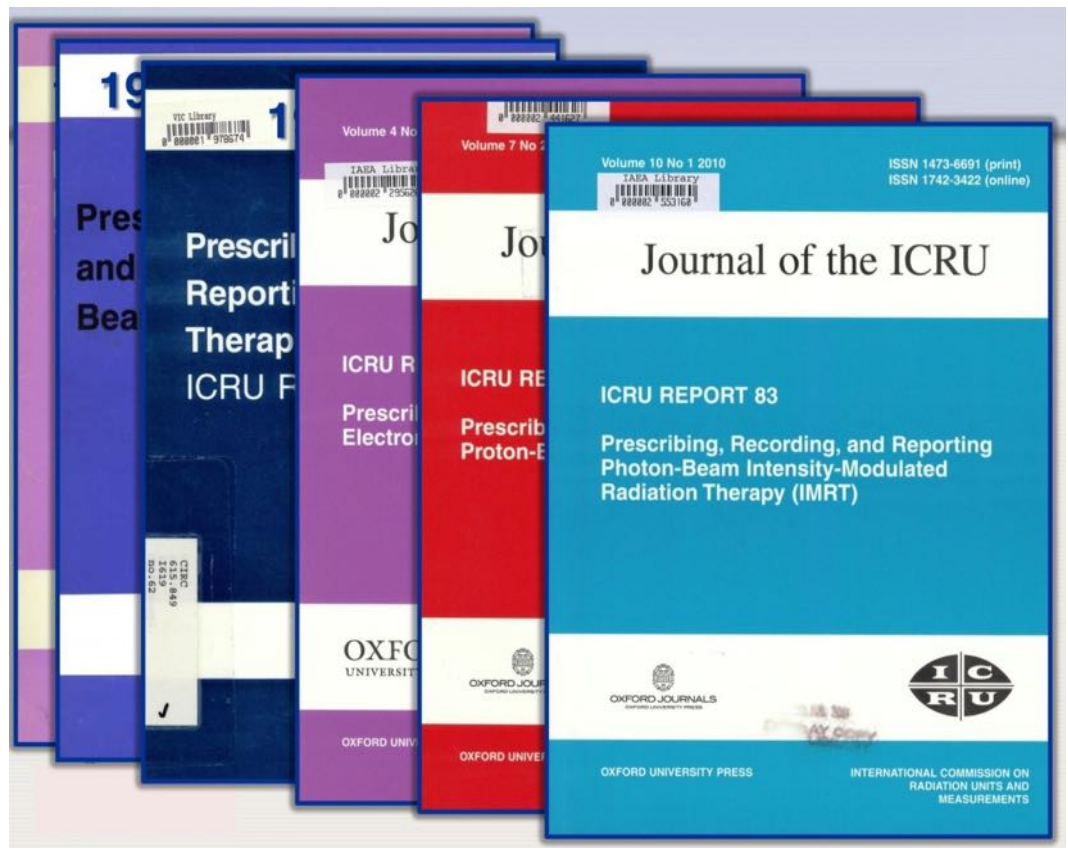
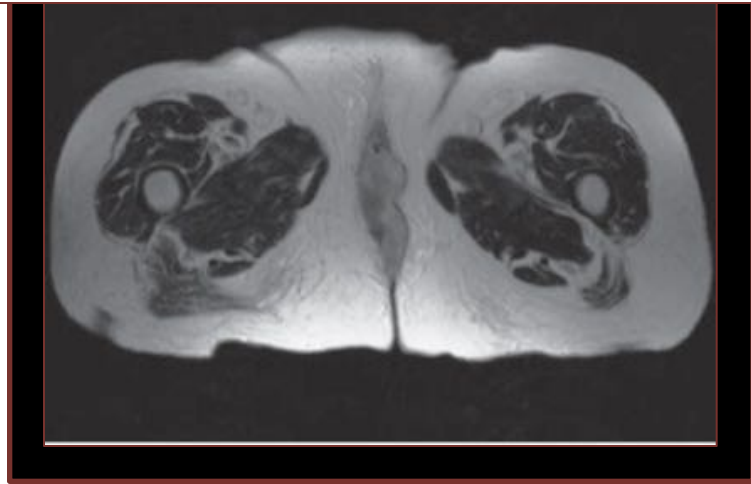
**Definitions of Target Volumes and Organs at Risk**

22 February 2011  
 Jacob (Jake) Van Dyk  
 Consultant, IAEA  
 Professor, University of Western Ontario, Canada



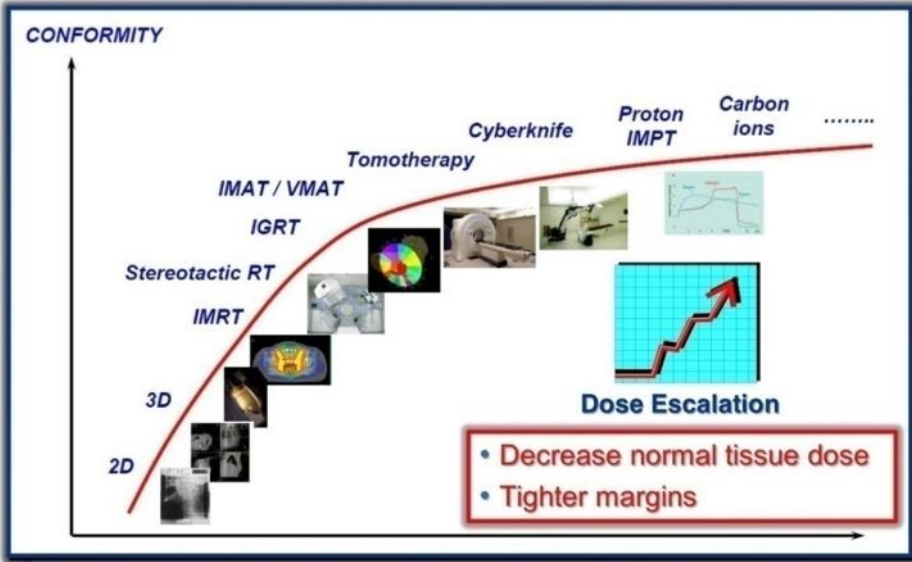
International Atomic Energy Agency

**Minimize collateral damage**

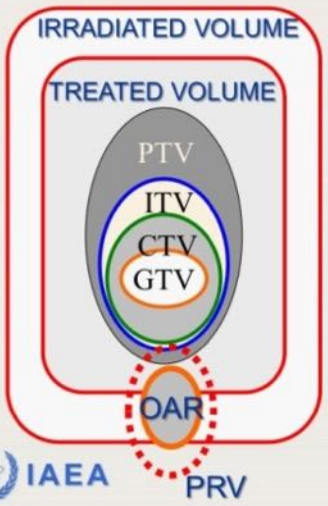


# Ca Vulva

## Evolution of Modern Radiation Therapy Technology



## Changes Over Time: ICRU 50 to 62



- PRV: Includes margin around the OAR to compensate for changes in shape and internal motion and for set-up variation.

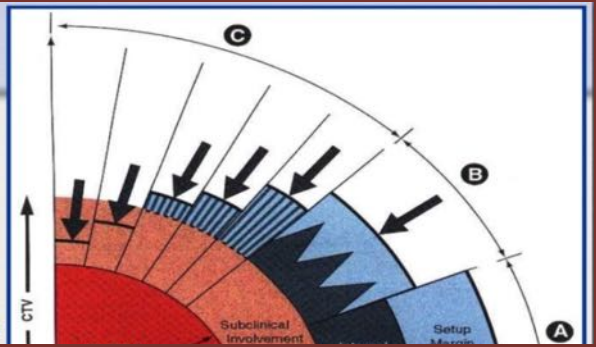
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## Margins

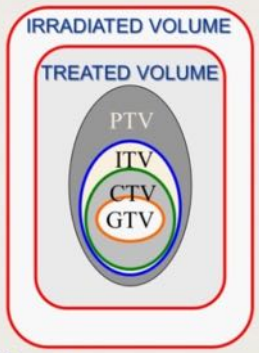
- A.**  
 $PTV = CTV + IM + SM$
- B.**  
 $PTV = CTV + \sqrt{IM^2 + SM^2}$
- C.**

“Global” safety margin

- Accounts for
  - OAR
  - Decrease of subclinical spread from GTV



## Note ...



We may be able to reduce technical margins ...  
 but **not biological margins**

## ICRU 83 Purpose

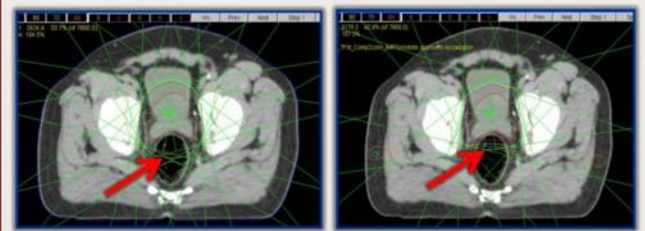
2010



- Irradiation techniques have advanced
  - 3-D CRT to IMRT
  - More availability of CT
  - Additional imaging – CT + MRI, PET, PET/CT, functional
  - Improved conformity
    - Reduced doses to normal tissues
  - More detailed dose-volume information on TPS

## Convex vs Concave

- Careful definition of the concavity is more important for IMRT than for 3-D CRT





# Ca Vulva

***(Stage II) LN-, Simple Vulvectomy -> 50 Gy with 6-18 MV photons and appropriate bolus***

***(Stage II) negative margins -> Perineal electron beam boost to bring vulva excision site dose to 60 Gy***

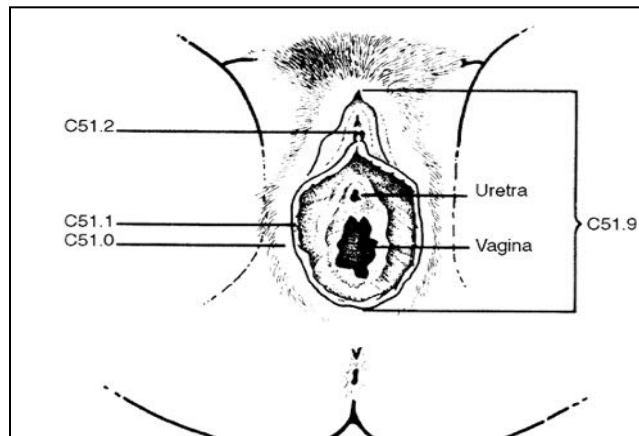
***(Stage II) positive margins -> After 60 Gy, additional boost to positive margins or positive lymph nodes (5 Gy) with electrons or interstitial implant***

***(Stage IV) Pre-operative irradiation -> 50 Gy to vulva or inguinal areas; boost to positive margins (10-15 Gy) via perineal portal or interstitial implant; boost to inguinal region via AP field (10-15 Gy)***

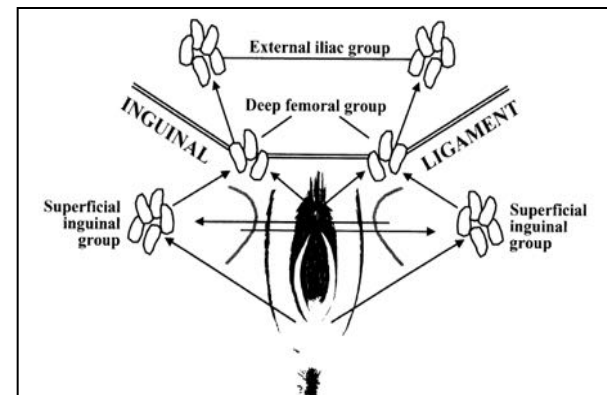
***(Stage IV) Post-operative irradiation -> boost to primary tumor (10-15 Gy) via interstitial and/or intracavitary and/or appositional electrons, when indicated***

# Ca Vulva

## PATTERN OF SPREAD AND FAILURE



- **LABIA**
- **CLITORIS**
- **PERINEUM**
- **URETHRA**
- **ANUS**
- **VAGINA**



- **SUPERFICIAL INGUINO-FEMOR LFN**
- **DEEP INGUINO-FEMORAL LFN**
- **EXTERNAL ILIAC LFN**



# Ca Vulva

**APPROPRIATE DELINEATION OF CLINICAL VOLUMES IS A CRITICAL FACTOR REQUIRING A PROPER KNOWLEDGE OF GTV, CTVs AND OARs**

# Ca Vulva

**GTV**

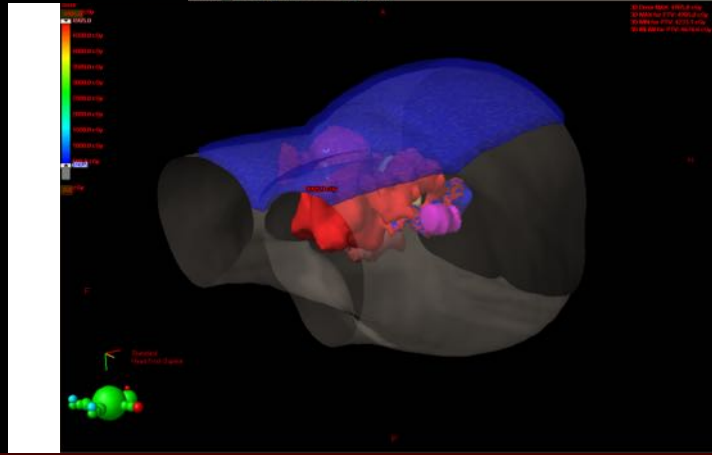
gross disease

**CTV-T**

vulva + margin

**PTV**

CTV + margin



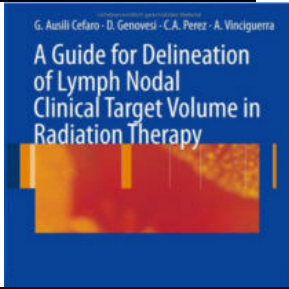
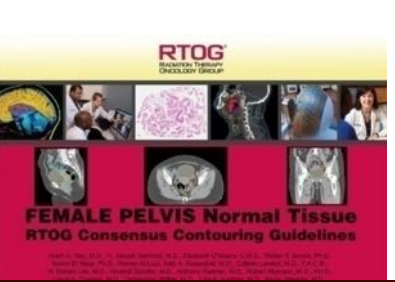
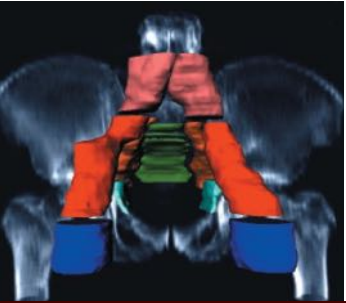


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## CTV-N

Disease Status	PAN	CIN	IIN	EIN	IGN
> One IGN positive	-	-	+	+	+
Pelvic node positive	-	+	+	+	+

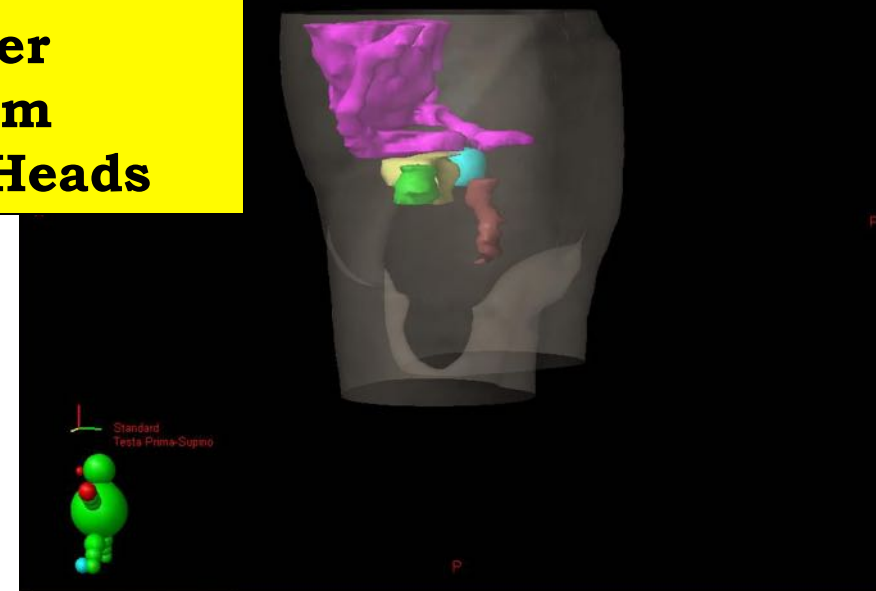
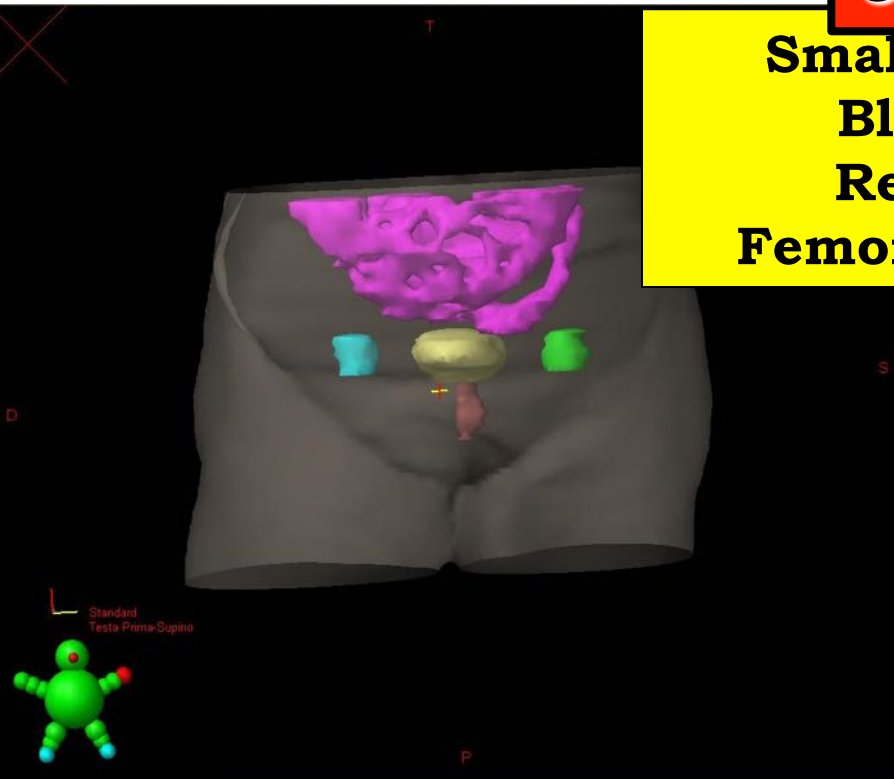
**PAN:** para-aortic LFN; **IIN:** internal iliac LFN;  
**CIN:** common iliac LFN; **EIN:** external iliac LFN;  
**IGN:** inguinal LFN



# Ca Vulva

## OARs

Small Bowell  
Bladder  
Rectum  
Femoral Heads





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**What technique???**

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doi:10.1016/j.ijrobp.2005.11.007

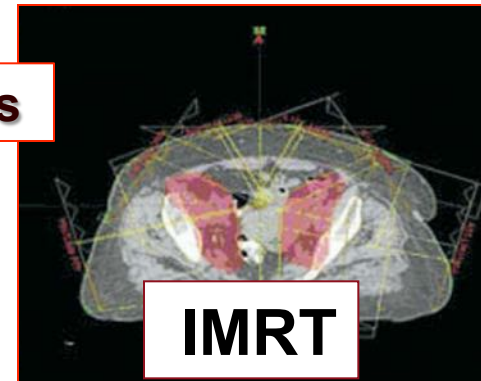
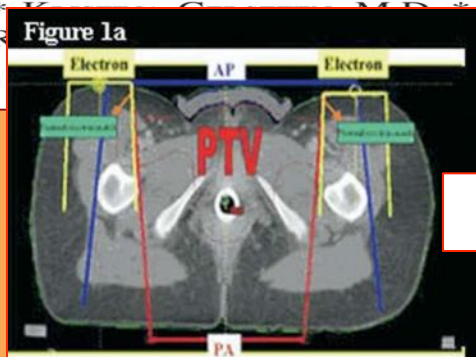
**S. Beriwal et al., 2006**

**CLINICAL INVESTIGATION**

**Vulva**

**INTENSITY-MODULATED RADIOTHERAPY FOR THE TREATMENT OF VULVAR CARCINOMA: A COMPARATIVE DOSIMETRIC STUDY WITH EARLY CLINICAL OUTCOME**

SUSHIL BERIWAL, M.D.,\* DWIGHT E. HERON, M.D.,\* HAYEON KIM, M.S.,\* GWENDOLYN KING, M.S.,\*  
 JEFFREY SHOGAN, M.D.,\* SANJEEV BAHRI, M.D.,\* KENNETH G. COOPER, M.D.,\* JOE LEE, PH.D.,†  
 JOSEPH KELLEY, M.D.,\* AND RICHARD W. PORTER, M.D.,\*  
 \*University of Pittsburgh Cancer Institute, Pittsburgh, PA; †University of Pittsburgh Medical Center, Pittsburgh, PA



**VS**

**9 pz 3DCRT**  
 Photons Field: AP-PA  
 Electron Field : Inguinal L-R

**IMRT**

- **PATIENTS:**  
 15 Stage II- IVA
- **RT:**  
 7 IMRT Pre-Op CRT (5FU-CDDP)  
 8 IMRT Post-Op
- **Median Dose:**  
 46.4 Gy Pre-Op  
 50.4 Gy Post-Op



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 JOSEPH KELLEY, M.D.,\* AND ROBERT P. EDWARDS, M.D.\*

\*University of Pittsburgh Cancer Institute, Pittsburgh, PA; and <sup>†</sup>D3 Advanced Radiation Planning, Pittsburgh, PA

GTV	CTV-T	CTV-N	PTV	OAR
GROSS DISEASE	VULVA + 1 CM MARGIN O ANY GTV + 1 CM MARGIN	BIL. EIN BIL. IIN IGN + 1-2 CM MARGIN	CTV + 1 CM	SMALL BOWELL BLADDER RECTUM FEMORAL HEADS

# Ca Vulva



**S. Beriwal et al., 2006**

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Table 3. Volume of critical structures receiving greater than 30 Gy (V30)

Organ	IMRT	3D	Reduction (%)	p Value
Rectum	45%	87%	41%	0.1
Bladder	62%	88%	26%	0.04
Small bowel	44%	71%	27%	0.3

**Femoral head:**

mean of maximum dose : **49.50 ± 3.1 Gy** with IMRT

mean of maximum dose : **50.17 ± 4.4 Gy** with 3DCRT



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SUSHIL BEF  
 JEFFREY

\*Univ

Table 4. Acute gastrointestinal, bladder, and skin toxicity

RTOG grade	0	1	2	3	4
Gastrointestinal	2	9	3	1	0
Bladder	12	1	2	0	0
Skin	0	4	11	0	0



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Official Journal of the American Society for Radiation Oncology

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doi:10.1016/j.ijrobp.2009.02.066

**M. S. Moran et al., 2010**

## CLINICAL INVESTIGATION

### CLINICAL UTILITY OF THE MODIFIED SEGMENTAL BOOST TECHNIQUE FOR TREATMENT OF THE PELVIS AND INGUINAL NODES

M. S. MORAN, M.D.,\*† W. A. CASTRUCCI, M.D.,\* M. AHMAD, PH.D.,\*†  
H. SONG, PH.D.,\* M. W. LUND, M.A., C.M.D.,† S. M.  
DANIEL CHAMBERLAIN, M.D.,\* AND S. A. HIGGINS

\*Yale University School of Medicine, Department of Therapeutic Radiology, New Haven, Connecticut and William W. Backus Hospital, Norwich, Connecticut

Clinical parameters	No. of patients
Primary anal cancer	11
Stage II	6
Stage IIIA/IIIB	5
Vulvar cancer	15
Stage II	3
Stage III	6
Stage IVA	4
Recurrent	2
Rectal cancer	3
Stage IIB	3
Vaginal cancer	6
Stage IIA	1
Stage IIIB	2
Stage IVA	1
Recurrent vaginal*	2
Cervical cancer	2
Stage III	2

## • PATIENTS:

**May 2001 – March 2007**  
**37 RT pelvis and inguinal nodes**  
**32 evaluable**  
**15 Vulvar Cancer Stage II - IVA**





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\*Yale University School of Medicine, Department of Therapeutic Radiology, New Haven, Connecticut and William W. Backus Hospital, Norwich, Connecticut

Concomitant chemotherapy	
Yes	31
5-FU/MMC	10
5-FU alone	4
CDDP	13
Carbo/taxol	1
Unknown	3
No	6
Total dose	
<45 Gy	5
≥45 Gy to 50.4 Gy	30
>50.4 Gy	2

Abbreviations: 5-FU = 5 Fluoro-Uracil; MMC = Mitomycin C; CDDP = cisplatinum.

**•RT:**  
**MSBT (Modified Segmental Boost Technique)**

**•Total Median Dose:**  
**45 Gy – 50.4 Gy**

**Dosimetric Comparison of MSBT vs IMRT**

**Five randomly chosen patients who had undergone MSBT**

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**CLINICAL INVESTIGATION**

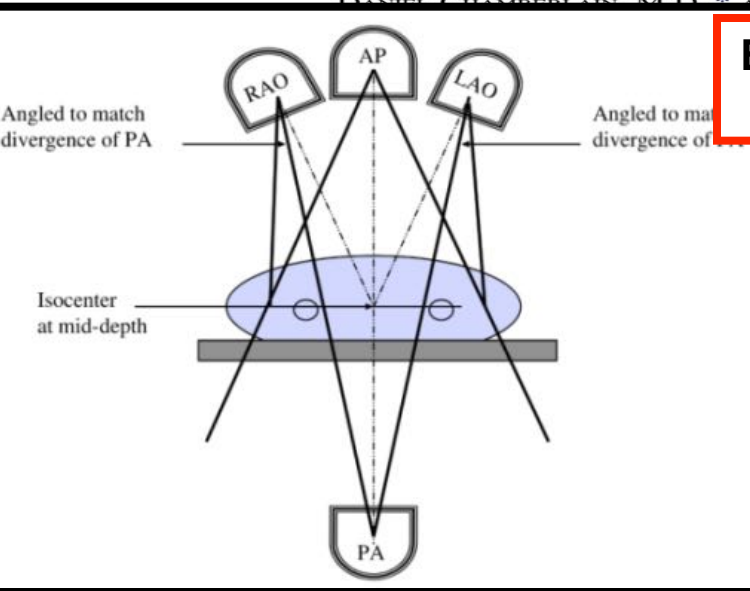
**CLINICAL UTILITY OF THE MODIFIED SEGMENTAL BOOST TECHNIQUE FOR TREATMENT OF THE PELVIS AND INGUINAL NODAL REGIONS IN**

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aven Hospital,

**Beam arrangements for the MSBT**



- A wide anteroposterior (ap) photon field
  - A narrow posteroanterior (pa) pelvic field
  - A bilateral (or unilateral) inguinal boost field(s).
- The inguinal fields are angled slightly to align with the divergence of the PA field and are shaped by the MLCs to boost the inguinal region

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 An International Journal

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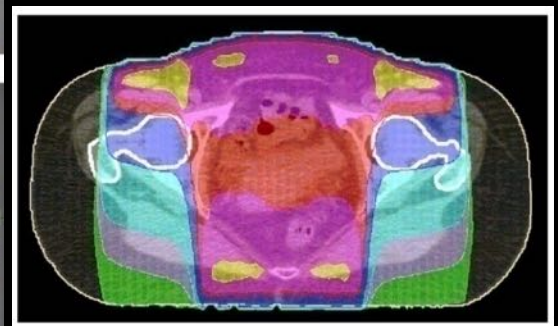
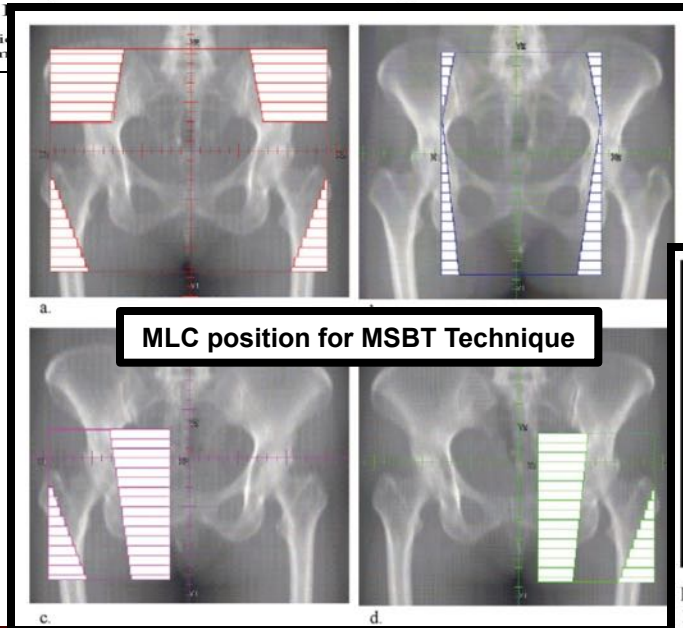
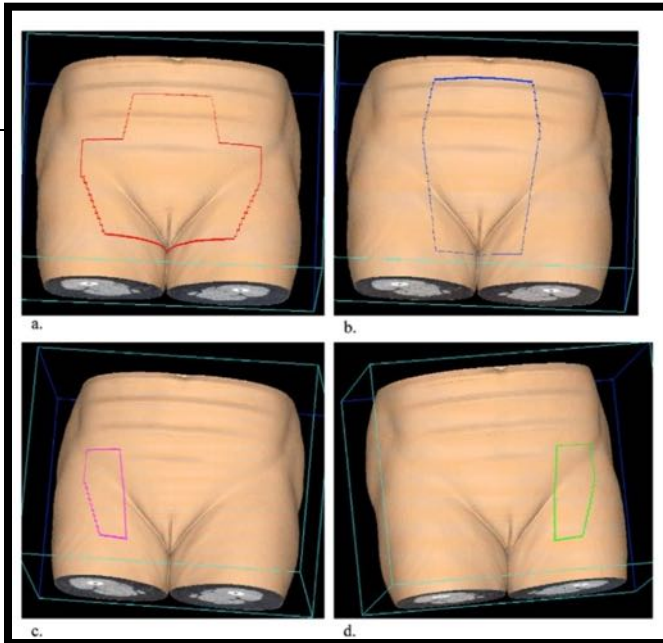


Fig. 4. Typical isodose distribution for the MSBT. 110% = yellow; 105% = pink; 100% = red; 80% = dark blue; 60% = light blue; 40% = lavender; 20% = green. The femoral heads are outlined in white.

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**CLINICAL INVESTIGATION**

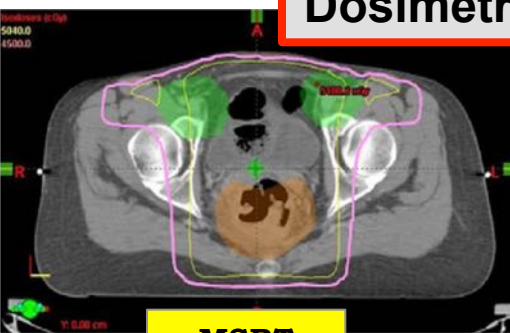
**CLINICAL UTILITY OF THE MODIFIED SEGMENTAL BOOST  
 FOR TREATMENT OF THE PELVIS AND INGUINAL N**

**M. S. Moran et al., 2010**

**Dosimetric Comparison**

5 patients

**DVHs**  
 Bladder  
 Marrow  
 Rectum  
 Small bowel



**VS**

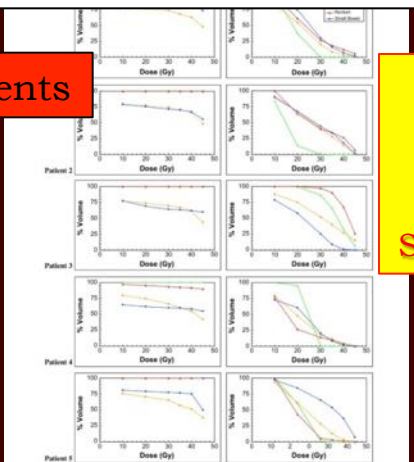


Fig. 7. Dose volume histogram (DVH) plots comparing doses delivered to bladder, marrow, rectum, and small bowel for MSBT and IMRT plans (5 patients).

**FEMORAL HEAD DOSES ( 10 patients)**  
 median **V45**: 6.5% (1% to 13%)  
 median **V27.5**: 86.5% (68% to 97%)  
 median **dmax**: 107.5% (102% - 118%)

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Table 5. Mean doses to Organs at Risk for 5 Patients Treated with MSBT versus IMRT\*

Dose (Gy)	Bladder vol mean % (range %)				Rectum vol mean % (range %)				Bone marrow vol mean % (range %)				Small bowel vol mean % (range %)			
	MSBT		IMRT		MSBT		IMRT		MSBT		IMRT		MSBT		IMRT	
10	100	(100-100)	96.7	(83.7-100)	99.4	(97.2-100)	94.8	(76.7-100)	78.7	(75.6-82.0)	87.1	(79.8-93.6)	80	(65.1-97.3)	87.6	(72.7-99.7)
20	100	(100-100)	41.2	(14.1-99.8)	99	(95.1-100)	58.9	(26.3-100)	74.7	(70.4-77.5)	61.2	(47.7-75.0)	76.4	(62.2-96.0)	69.1	(57.9-84.6)
30	100	(100-100)	17.5	(0-86.1)	98.7	(93.3-100)	36.6	(5.7-97.1)	70	(63.3-74.4)	31.6	(17.5-51.9)	73.8	(60.1-95.0)	37.2	(20.5-65.6)
35	100	(100-100)	13.1	(0-65.7)	98.5	(92.4-100)	31.1	(3.2-90)	64.7	(57-70.7)	20.1	(8.5-40.2)	72.8	(59.6-94.5)	24.3	(3.2-54.0)
40	100	(100-100)	6.6	(0-33.2)	98.3	(91.4-100)	22.4	(0.9-67.9)	59.4	(51.1-66.1)	10.2	(1.2-27.4)	71.4	(58.5-93.6)	13.1	(1.3-37.0)
45	100	(100-100)	1.3	(0-6.3)	97.9	(89.6-100)	7.7	(0-26.0)	44	(43.96-48.5)	4	(0.0-15.5)	58.8	(50.0-73.6)	2	(0.1-7.3)

\* Data show mean OAR volumes for selected dose levels of 10, 20, 30, 35, 40, 45 Gy for optimized MSBT vs. IMRT plans for five patients.



# Ca Vulva



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\* Yale University School of Medicine, Department of Therapeutic Radiology, New Haven, Connecticut; and † Yale New Haven Hospital, New Haven, Connecticut and William W. Backus Hospital, Norwich, Connecticut

**THE MSBT DELIVERS A MEAN PRESCRIBED DOSE TO :**

**100% OF THE BLADDER**

**98% OF THE RECTUM**

**59% OF THE SMALL BOWEL**

**44% OF THE BONE MARROW**

**THE MSBT PLAN ARE SIGNIFICANTLY HIGHER DOSES THAN THE MEAN DOSES  
DELIVERED WITH THE IMRT PLAN**



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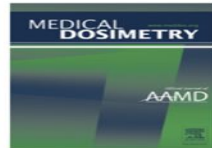
Medical Dosimetry 37 (2012) 310-313

**M. C. W. M. Bloemers et al., 2012**



Medical Dosimetry

journal homepage: [www.meddos.org](http://www.meddos.org)



A dosimetric evaluation of dose escalation for the radical treatment of locally advanced vulvar cancer by intensity-modulated radiation therapy

Monique C.W.M. Bloemers, M.D.,\*† Lorraine Portelance, M.D.,† Russell Ruo, M.Sc.,‡ William Parker, Ph.D.,‡ and Luis Souhami, M.D.†

\*Department of Radiotherapy, the Netherlands Cancer Institute, Amsterdam, the Netherlands

‡McGill University

**• PATIENTS: 10 with Vulvar Cancer**  
**5 RT Post-Operative**  
**5 RT Definitive**

## Post-Operative Group

CTV1	PTV1	OAR
Low common iliac BIL. EIN IIN IGN Surgical vulvar bed	7-mm margin around the CTV1	Bladder Small bowell Rectum Femoral heads



# Ca Vulva

Medical Dosimetry 37 (2012) 310-313

**M. C. W. M. Bloemers et al., 2012**

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A dosimetric evaluation of dose escalation for the radical treatment of locally advanced vulvar cancer by intensity-modulated radiation therapy

Monique C.W.M. Bloemers, M.D.,\*† Lorraine Portelance, M.D.,† Russell Ruo, M.Sc.,‡ William Parker, Ph.D.,‡ and Luis Souhami, M.D.†

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**• PATIENTS: 10 with Vulvar Cancer**  
**5 RT Post-Operative**  
**5 RT Definitive**

**Definitive Group**

	<b>GTV</b>	<b>CTV1</b>	<b>PTV1</b>	<b>PTV2</b>	<b>OAR</b>
	<b>primary tumor</b>	<b>BIL EIN</b>	<b>7-mm margin</b>	<b>7-mm margin</b>	<b>Bladder</b>
	<b>clinically</b>	<b>IIN</b>	<b>around the</b>	<b>around the</b>	<b>Small bowell</b>
	<b>involved nodes</b>	<b>IGN</b>	<b>CTV1</b>	<b>GTV</b>	<b>Rectum</b>
		<b>Margin tumor</b>			<b>Femoral heads</b>





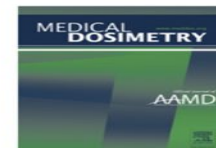
# Ca Vulva

Medical Dosimetry 37 (2012) 310-313

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## Post-Operative Group

3D-CRT

PTV1

45 Gy/25 fr × 1.8 Gy

IMRT

PTV1

45 Gy/25 fr × 1.8 Gy



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Health Centre, Montreal, Quebec, Canada

## Definitive Group

**3D-CRT**

PTV1

50.4 Gy/28 fr × 1.8 Gy

PTV2

6 Gy/3 fr × 2.0 Gy

**Seq-IMRT**

PTV1

50.4 Gy/28 fr × 1.8 Gy

PTV2

6 Gy/3 fr × 2.0 Gy

**SIB-IMRT**

PTV1

50.4 Gy/28 fr × 1.8 Gy

PTV2

56.0 Gy/28 fr × 2.0 Gy

**SIB-IMRT-esc**

PTV1

50.4 Gy/28 fr × 1.8 Gy

PTV2

67.2 Gy/28 fr × 2.4 Gy

†Department of Medical Physics, McGill University

‡Department of Medical Physics, McGill University



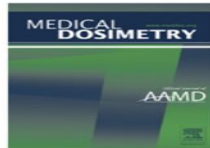
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**IMRT**

**Post-Operative Group**

M.D.,<sup>†</sup> Russell Ruo, M.Sc.,<sup>‡</sup> William Parker, Ph.D.,<sup>‡</sup>

and Luis Sou

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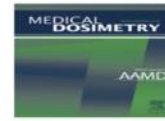
	Bladder	Small bowell	Rectum	Femoral heads
D mean	↓	↓	↓	↓
V30	↓	↓	↓	↓
V40	↓	↓	↓	↓
V45		↓	↓	↓

Mean Volume received doses >30 Gy with IMRT compared with 3D-CRT		
Small bowell	Bladder	Rectum
28%	51%	61%

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313



## Definitive Group

Comparison of dose distribution to OAR between 3D-CRT and IMRT in the def-group

	3D-CRT (TD 56.4 Gy)	IMRT-seq (TD 55.8 Gy)	IMRT-SIB (TD 56 Gy)	IMRT-SIB-esc (TD 67.5 Gy)
<b>Small bowel</b>				
Mean	44.85 Gy	31.44 Gy	31.36 Gy	29.63 Gy
D <sub>max</sub>	54.82 Gy	54.87 Gy	55.37 Gy	58.84 Gy
V30	84.56%	58.25%	59.77%	52.30%
V40	80.87%	26.27%	25.76%	20.86%
V45	78.21%	16.37%	15.69%	11.81%
<b>Rectum</b>				
Mean	54.42 Gy	37.62 Gy	37.19 Gy	39.52 Gy
D <sub>max</sub>	57.05 Gy	56.72 Gy	56.86 Gy	65.22 Gy
V20	100%	99.55%	99.13%	97.93%
V30	100%	66.33%	59.52%	61.97%
V40	100%	35.34%	39.18%	38.51%
V45	100%	29.11%	29.95%	33.29%
<b>Bladder</b>				
Mean	53.32 Gy	34.93 Gy	36.79 Gy	36.82 Gy
D <sub>max</sub>	56.20 Gy	60.15 Gy	57.86 Gy	73.75 Gy
V30	100%	65.26%	69.76%	60.97%
V40	100%	29.46%	38.79%	37.87%
V45	100%	18.03%	26.33%	29.41%
<b>Left femur</b>				
Mean	50.02 Gy	27.15 Gy	27.18 Gy	25.52 Gy
V30	96.94%	30.89%	30.6%	27.96%
V45	89.14%	1.15%	1.78%	1.01%
<b>Right femur</b>				
Mean	50.82 Gy	27.19 Gy	27.14 Gy	25.96 Gy
V30	98.01%	32.08%	31.16%	30.27%
V45	90.57%	1.63%	2.77%	3.31%

**SIB-IMRT-esc**  
*increased D<sub>max</sub> for*  
**SMALL BOWEL**  
**RECTUM**  
**BLADDER**

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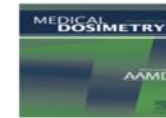
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**M. C. W. M. Bloemers et al., 2012**

313

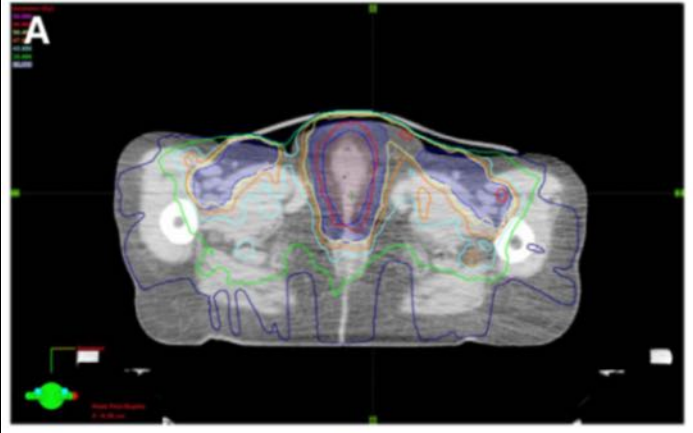
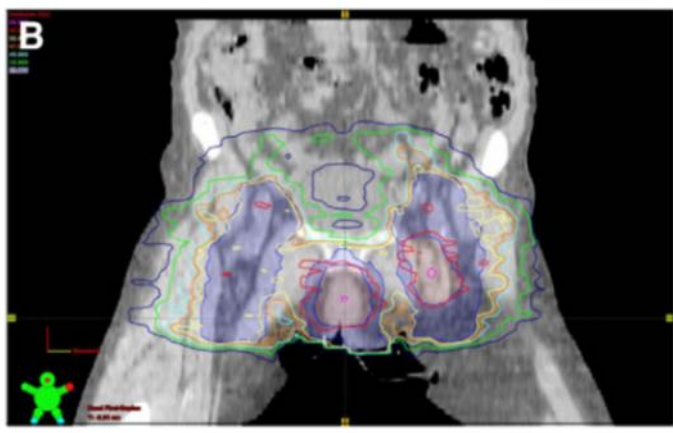
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iversity

**Fig. 1.** Dose distribution. (A) Axial and (B) coronal view obtained with a SIB-IMRT technique to a TD of 56 Gy. The isodose lines are in terms of 95% (orange) and 70% (green) of the (elective) prescription dose of 50.4 Gy. The red isodose line: 95 % of prescription dose of PTV2 (TD 56 Gy). The blue and pink contours represent PTV1 and PTV2, respectively.

- **IMRT** -> reduces acute and late toxicity to the OAR
- **SIB-IMRT** -> higher fractional boost doses



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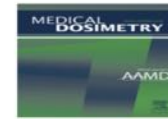
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313



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- **Seq-IMRT** and **SIB-IMRT** plans: -> equivalent dosimetrically for normal tissue sparing
- **Locoregionally advanced vulvar cancer** -> dose escalation (62–64 Gy) to the tumor seems to be necessary to optimize tumor control
- **SIB-IMRT** and **SIB-IMRT-esc.** -> No significant differences for rectal, bladder, and femoral head sparing between
- **SIB-IMRT** -> For the small bowel, differences for the V30, V45, and Dmean is in favor
- **SIB-IMRT-esc** -> a fractional boost dose of 2.4 Gy/fraction was evaluated



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## CONCLUSION

- **Correct identification of clinical volumes**  
Knowledge of the natural history of the disease  
Assisting atlases contouring
- **Best technique**  
IMRT is the ideal technique of treatment:
  - reduction of acute and late toxicity of the rectum, bladder, femoral heads and small intestine
  - possibility of dose escalation and SIB



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**THE FUTURE IS NOT  
ONLY REPRESENTED  
BY MACHINES BUT  
FROM TEAM  
EXPERIENCE!!**

**EXPERIENCE!!  
FROM TEAM**