



Associazione
Italiana
Radioterapia
Oncologica

Genova, 19-22 Novembre 2011
Porto Antico di Genova
Centro Congressi

ESISTE UN'ALTERNATIVA ALLA BRACHITERAPIA IN GINECOLOGIA ONCOLOGICA?

**Vitaliana De Sanctis
Cattedra di Radioterapia
Facoltà di Medicina e Psicologia
Università
"Sapienza"
Roma**

**RADIUM THERAPY
IN CANCER**

AT THE MEMORIAL HOSPITAL
NEW YORK

1917 REPORT

BY
HENRY H. JANNEY, M.D.

WITH THE ASSISTANCE OF THE
STAFF AND FACULTY
OF THE MEMORIAL HOSPITAL, N. Y.

AND THE ASSISTANCE OF THE STAFF OF THE
MEMORIAL HOSPITAL, N. Y.



NEW YORK
PAUL B. HOEBER
1917

the tumor and infection, but these inoperable cases were regarded as operable after the treatment. Wickham and Dognin took up the problem of filtration and introduced tubes with a small thickness of 2.0015 mm of lead. They were also the first to introduce systematic cross-filtration. By 1913, Chason and Rubens-Dorel had treated a large number of patients with cervical carcinoma using larger doses of radium than before, and demonstrated the necessity of a stronger filtration when the radium content of the application was increased. Among 50 inoperable cases, they obtained clinical cure of the growth affecting the cervix in 26 cases. The subsequent years brought further reports mainly from England and Lacaze-Gagneur, who painstakingly perfected techniques and dosimetry for intracavitary applications of radium for cancer of the cervix (Figure 9).



Figure 8. Cover of book entitled, "Radium Therapy in Cancer" by Janney, et al. (1917).

Radium Treatment of Uterine Cancer

Wickham, by 1906, had introduced the use of radium in the treatment of cancer. He began his work in 1906, the results of the treatment of a few cases in 1910 and 1911.¹¹

In France

In 1907, Dognin demonstrated biological effects of the rays emanated by radium salt and found that the superficial burn caused by a radioactive substance was due to beta and soft alpha rays. In 1909, Dognin reported that in 25% of the inoperable cases of cancer he had obtained such local

OS range 43%-77%

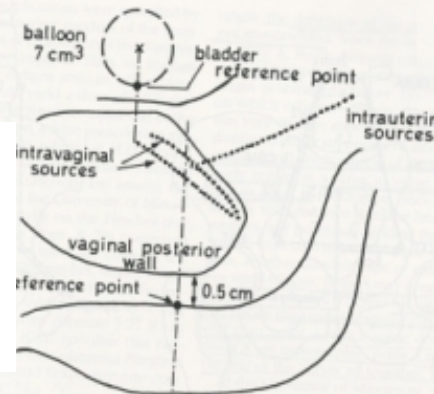
LC range 65%-91%

TOXICITY range 1.4%-73%

G3-G5 < 3%

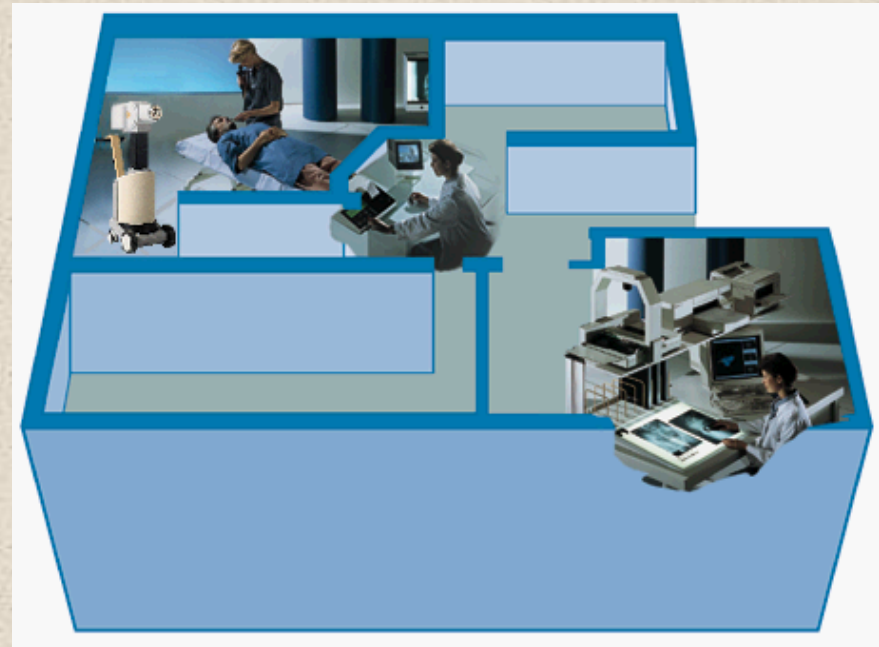
International Commission on Radiation Units and Measurements (ICRU), Dose and volume specifications for reporting intracavitary therapy in gynecology. Bethesda, MD: ICRU, 1985. ICRU Report no. 38.

Figure 9. The Pons System (originally developed by Dognin) of intracavitary application.

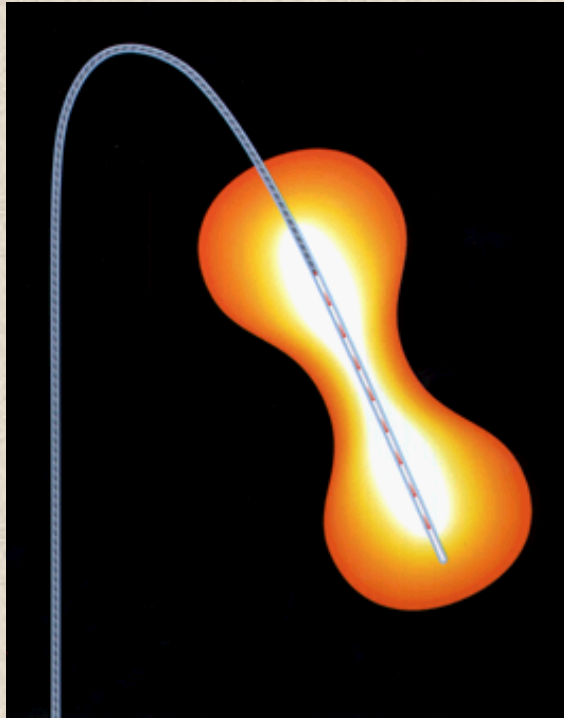


time of brachytherapy. A dose prescribed to point A would always result in a fixed dose at a fixed distance from the cervical os, regardless of the size or shape of the residual mass at the time of brachytherapy. Exophytic tumors that respond

Remote afterloading



Hashimoto S. Intracavitary radiotherapy using remote afterloading technique (author's translation). *Radioisotopes* 1980;29(2):103-10.



HDR

Henschke UK, Hilaris BS, Mahan GD. Intracavitary radiation therapy of cancer of the uterine cervix by remote afterloading with cycling sources. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* 1966;96(1):45-51.

O'Connell D, Howard N, Joslin CA, Ramsey NW, Liversage WE. A new remotely controlled unit for the treatment of uterine carcinoma. *Lancet* 1965;2(7412):570-1.



ELSEVIER

Radiotherapy and Oncology 74 (2005) 223–225

**RADIOTHERAPY
& ONCOLOGY**

JOURNAL OF THE EUROPEAN SOCIETY FOR
THERAPEUTIC RADIOLOGY AND ONCOLOGY

www.elsevier.com/locate/radonline

Editorial

Brachytherapy: a new era

Jean-Jacques Mazon

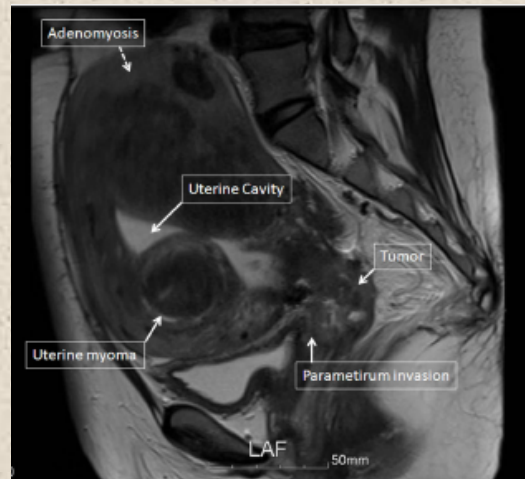
Department of Radiation Oncology, Groupe Hospitalier Pitié-Salpêtrière, AP-HP, 47-83, Boulevard de l'Hôpital, 75651 Paris cedex 13, France

Received 28 January 2005; received in revised form 2 February 2005; accepted 4 February 2005

**HIGH-DOSE-RATE BRACHYTHERAPY—HIGH-DOSE, HIGH-TECH,
AND HIGH RESULTS**

DANIEL G. PETEREIT, M.D.,*† AND JACK F. FOWLER, PH.D.*

Image-guided brachytherapy



Imaging Technologies for High Dose Rate Brachytherapy for Cervical Cancer: A Systematic Review¹

D. D'Souza ^{*}, F. Baldassarre [†], G. Morton [‡], C. Falkson [§], D. Batchelar ^{||}

Clinical Oncology xxx (2011) 1–16

Accessibility, ease of use and ability to define anatomy of different imaging technologies for definitive treatment planning

Imaging technology	Accessibility	Ease of use	Ability to define anatomy/positioning of applicators
Fluoroscopy	☆☆☆	☆☆☆	*
Ultrasound	☆☆☆	☆☆☆	NA
Computed tomography	☆☆	☆☆☆	☆☆
Magnetic resonance imaging	*	☆☆	☆☆☆
Positron emission tomography	*	*	NA

Accessibility: * = not accessible in brachytherapy room; ** = variable accessibility; *** = accessible within the brachytherapy room.

Ease of use: * = difficult to use; ** = variable ease of use; *** = easy to use.

Ability to define anatomy with respect to positioning of applicators: * = insufficient evidence of ability to define anatomy to ensure the sparing of healthy surrounding tissues while delivering a therapeutic dose to the tumour; ** = some evidence shows an ability to visualise anatomy is sufficient in certain areas and less so in others; *** = excellent visualisation of anatomy. NA = not applicable because this technology is not used in the definitive planning phase of brachytherapy.

This is the first systematic review assessing the use of different imaging technologies in brachytherapy for cervical cancer. The evidence supports the use of three-dimensional planning with computed tomography or MRI over conventional two-dimensional planning with fluoroscopic imaging, as there is improved anatomical delineation of structures and a more accurate assessment of volumetric doses. Limited clinical data suggest better tumour control and reduced toxicity, although more studies are required in this regard.

The use of magnetic resonance imaging for image-guided brachytherapy

M Barkati, S Van Dyk, F Foroudi and K Narayan

Journal of Medical Imaging and Radiation Oncology 54 (2010) 137–141

Progress has been made in the delivery of brachytherapy, from low-dose rate (LDR) to high-dose rate (HDR) treatments, allowing for dose optimisation, conformal treatments, improved radiation protection, and improved accuracy and efficiency. Image-guided brachytherapy, incorporating spatial and temporal changes, is now possible with advanced imaging and treatment technology. This report reviews the evidence for the benefits of image-guided brachytherapy using magnetic resonance imaging (MRI), mainly for cervix and prostate cancer, but also possibilities for other tumour sites. It also emphasises the need for a dedicated MRI unit for brachytherapy.

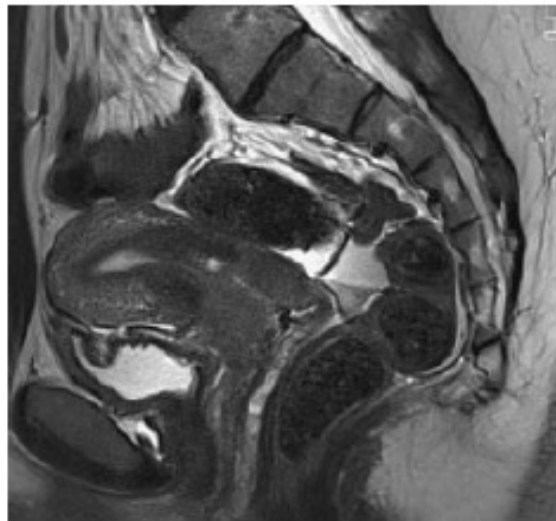


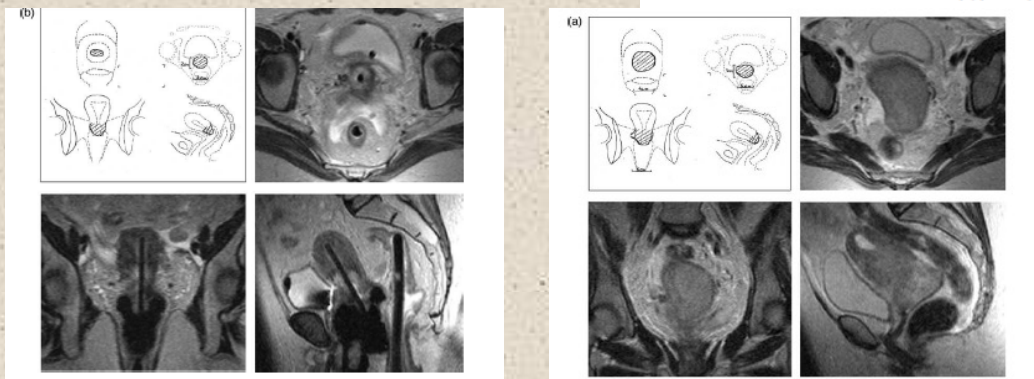
Fig. 1. T2-weighted MRI of cervix carcinoma (sagittal view).

- Accurate positioning of the applicator into the uterine cavity;
- Conformal dose distributions to target volume;
- Normal tissue sparing;
- Opportunity for dose escalation.

Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group[☆] (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV

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

Radiotherapy and Oncology 74 (2005) 235–245



Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy—3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology

Richard Pötter^{a,*}, Christine Haie-Meder^b, Erik Van Limbergen^c, Isabelle Barillot^d, Marisol De Brabandere^c, Johannes Dimopoulos^a, Isabelle Dumas^b, Beth Erickson^e, Stefan Lang^a, An Nulens^c, Peter Petrow^f, Jason Rownd^e, Christian Kirisits^a

Radiotherapy and Oncology 78 (2006) 67-77

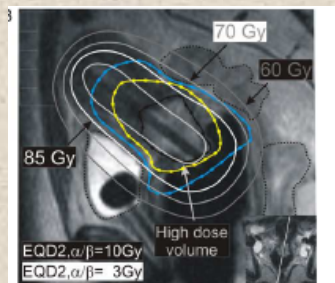


IMAGE GUIDED BRACHYTHERAPY

	Autore	Lindergaard, 2008	De Brabandere, 2008	Chargari, 2009	Kirisits, 2006
	N pts	85	56	45	141
	Punto A	77±5	81 ±7	71 ±6	79 ±10
CTV HR	Volume(cm3)	37	38	36	33
	D100	74 ±5	65 ±7	62 ±7	65 ±10
	D90	91 ±7	82 ±10	75 ±10	86 ±16
CTV IR	Volume (cm3)	113	105	90	92
	D100	60 ±3	58 ±5	54	53 ±3
	D90	68 ±3	69 ±6	64	66 ±9
Vescica	D2cm3	73	85	72	95
	Punto ICRU	67		64	72
Retto	D2cm3	65	63	61	65
	Punto ICRU	66		67	67
Sigma	D2cm3	68	66	61	62

COMPARATIVE STUDY OF LDR (MANCHESTER SYSTEM) AND HDR IMAGE-GUIDED CONFORMAL BRACHYTHERAPY OF CERVICAL CANCER: PATTERNS OF FAILURE, LATE COMPLICATIONS, AND SURVIVAL

KAILASH NARAYAN, F.R.A.N.Z.C.R.,* SYLVIA VAN DYK, DIP APP SCI,*
 DAVID BERNshaw, F.R.A.N.Z.C.R.,* CHRISHANTHI RAJASOORIYAR, M.D.,* AND
 SRINIVAS KONDALSAMY-CHENNAKESAVAN, M.P.H.^{††}

Int. J. Radiation Oncology Biol. Phys., Vol. 74, No. 5, pp. 1529–1535, 2009

Table 1. Patient characteristics by brachytherapy

Factors	LDR (n = 90)	HDRc (n = 127)
Age, median (range), y	60 (22–87)	55 (27–86)
International Federation of Gynecology and Obstetrics stages		

Table 4. Late toxicities and their rates by types of brachytherapy

	Bladder			Bowel			Vagina		
	Rate/100 person-years of follow-up			Rate/100 person-years of follow-up			Rate/100 person-years of follow-up		
	LDR	HDRc	HR (95% CI)	LDR	HDRc	HR (95% CI)	LDR	HDRc	HR (95% CI)
1	3.2	2.8	1.02 (0.41–2.54)	9.4	7.9	0.67 (0.39–1.15)	13.4	10.8	0.68 (0.41–1.13)
2	2.7	1.4	0.43 (0.14–1.27)	4.5	1.6	0.33 (0.11–0.94)	12.9	3.4	0.22 (0.11–0.46)
3 and 4	0.7	0.6	0.62 (0.09–4.09)	1.6	0.6	0.38 (0.07–2.08)	4.6	1.7	0.33 (0.11–0.98)

Abbreviations: LDR = low-dose rate; HDRc = conformal high-dose rate; HR = hazard ratio for HDRc relative to LDR. Numbers in bold represent a statistically significant difference.

Conclusions: Image-guided HDRc planning led to a large decrease in late radiation effects in patients treated by HDRc. Patterns of failure and survival were similar in patients treated either by LDR or HDRc. Crown Copy-

Clinical impact of MRI assisted dose volume adaptation and dose escalation in brachytherapy of locally advanced cervix cancer

Richard Pötter^{a,*}, Johannes Dimopoulos^a, Petra Georg^a, Stefan Lang^a,
 Claudia Waldhäusl^a, Natascha Wachter-Gerstner, Hajo Weitmann^a,
 Alexander Reinthaller^b, Tomas Hendrik Knocke^a, Stefan Wachter^a, Christian Kirisits^a

Radiotherapy and Oncology 83 (2007) 148–155

73 pts con 2D-BT
 72 pts con 3D-BT RM-based

T > 5 cm
CCR
LC

2D-BT 3D-BT
71% vs 90%
64% vs 82%

Tossicità a 3 anni G3-G4
10% 2D-BT vs 2% 3D-BT

Table 2
 Outcome at 3 years for 145 patients treated with 3D MRI based gynaecologic brachytherapy (dose escalation) and 3D conformal external beam therapy +/- simultaneous chemotherapy: events (n), patients per subgroup (n), actuarial estimates; p-values are given for large tumours to compare the two time periods and treatment approaches, respectively

	Overall 1998–2003			Period 1 1998–2000			Period 2 2001–2003		
	n events	n total	%	n events	n total	%	n events	n total	%
CCR true pelvis	14	138	88	10	70	83	4	68	93
2–5 cm	2	67	96	1	33	96	1	34	96
>5 cm	12	71	80	9	37	71*	3	34	90*
									p = 0.05
CCR pelvis	17	138	86	11	70	82	6	68	90
2–5 cm	5	67	91	2	33	93	3	34	89
>5 cm	12	71	80	9	37	71*	3	34	90*
									p = 0.05
PFS true pelvis	19	145	85	12	73	82	7	72	89
2–5 cm	1	67	98	0	33	100	1	34	96
>5 cm	18	78	73	12	40	64*	6	38	82*
									p = 0.09
PFS pelvis	22	145	82	13	73	80	9	72	87
2–5 cm	4	67	93	1	33	97	3	34	88
>5 cm	18	78	72	12	40	63*	6	38	81*
									p = 0.07
PFS distant	26	145	80	13	73	79	13	72	80
2–5 cm	7	67	88	4	33	87	3	34	90
>5 cm	19	78	71	9	40	71*	10	38	71*
									p = 1
PFS overall	48	145	64	26	73	62	22	72	67
2–5 cm	11	67	81	5	33	84	6	34	78
>5 cm	37	78	50	21	40	43*	16	38	57*
									p = 0.13
CS	43	145	68	25	73	62	18	72	74
2–5 cm	8	67	88	4	33	87	4	34	88
>5 cm	35	78	51	21	40	40*	14	38	62*
									p = 0.07
OS	59	145	58	34	73	53	25	72	64
2–5 cm	15	67	77	6	33	82	9	34	71
>5 cm	44	78	43	28	40	28*	16	38	58*
									p = 0.003

CCR: Continuous Complete Remission; PFS: Progression Free Survival; OS: Overall Survival, CS: Cancer Specific Survival.
 *p-value.

3D-CRT 45 Gy con CHT
3D-CRT 50.4 Gy senza CHT

BT 7 Gy x 4 malattia avanzata
BT 7 Gy x 5-6 malattia localizzata

Image-guided brachytherapy

**high-tech
brachytherapy** vs **high-tech
EBRT**

Clinical Application of Intensity-Modulated Radiotherapy for Locally Advanced Cervical Cancer

Brian D. Kavanagh,* Tracey E. Schefter,* Qiuwen Wu,† Shidong Tong,† Francis Newman,* Mark Arnfield,† Stanley H. Benedict,† Steve McCourt,* and Radhe Mohan†

Seminars in Radiation Oncology, Vol 12, No 3 (July), 2002: pp 260-271

Riduzione delle dosi ai tessuti sani

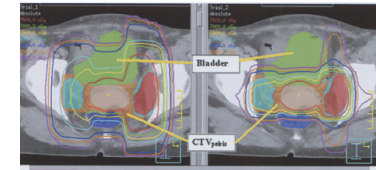
IMRT alternativa alla

Concomi integrati

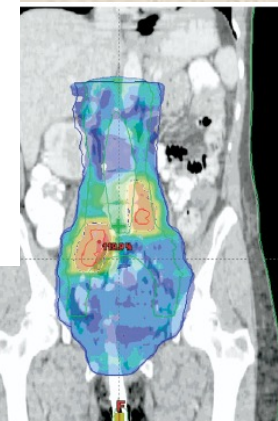
brachiterapia

Dose escalation

Riduzione del tempo totale di trattamento



1 dose distribution comparison: CXRT + BRT (left) versus IMRT + BRT (right). Rectangles below are the color of the isodose line encompassing the cumulative dose (cGy) noted inside the rectangle. bladder overlaps the CTV_{pelvic} anteriorly. Within the CTV_{pelvic} (not individually labeled) are the central pelvic nodal regions, and left-sided nodal boost volume. Abbreviations: CXRT, conventional external-beam; IMRT, intensity-modulated radiotherapy; BRT, brachytherapy.



APPLICATOR-GUIDED INTENSITY-MODULATED RADIATION THERAPY

DANIEL A. LOW, PH.D., PERRY W. GRIGSBY, M.D., JAMES F. DEMPSEY, PH.D., SASA MUTIC, M.S.,
JEFFREY F. WILLIAMSON, PH.D., JERRY MARKMAN, D.Sc.,¹ K. S. CLIFFORD CHAO, M.D.,
ERIC E. KLEIN, M.S., AND JAMES A. PURDY, PH.D.

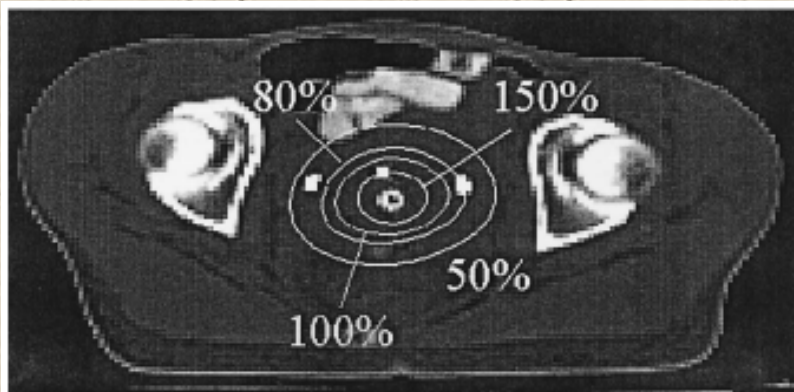
Int. J. Radiation Oncology Biol. Phys., Vol. 52, No. 5, pp. 1400–1406, 2002

applicatore Fletcher CT-compatibile

- 1) corretta localizzazione del target
- 2) limitare internal movement del tumore e degli organi a rischio

For these examples, the treatment plan parameters were to deliver 3800 cGy total dose to the target, and limit the bladder and rectum dose to no more than 3800 cGy, based on 6 intracavitary insertions.

BT-HDR



IMRT

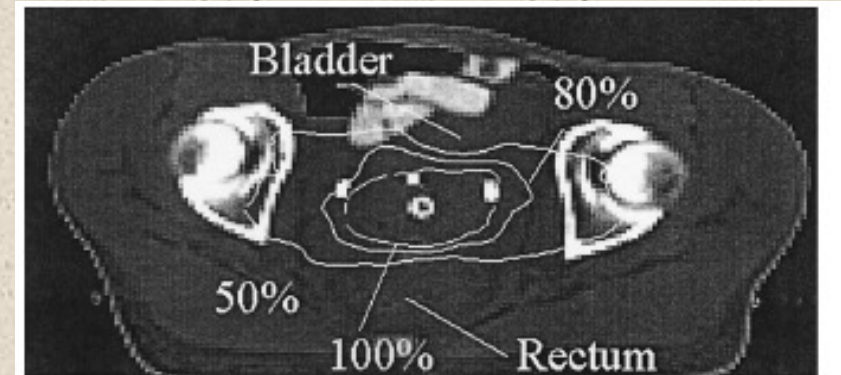
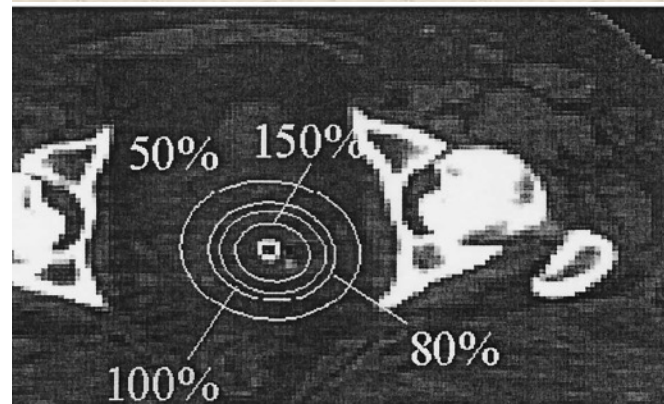
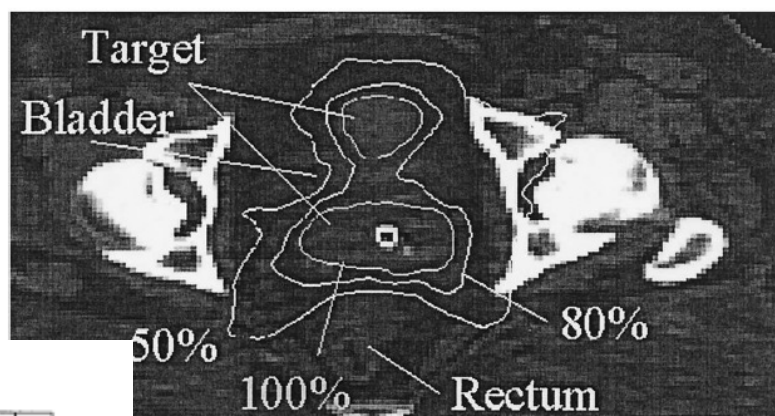
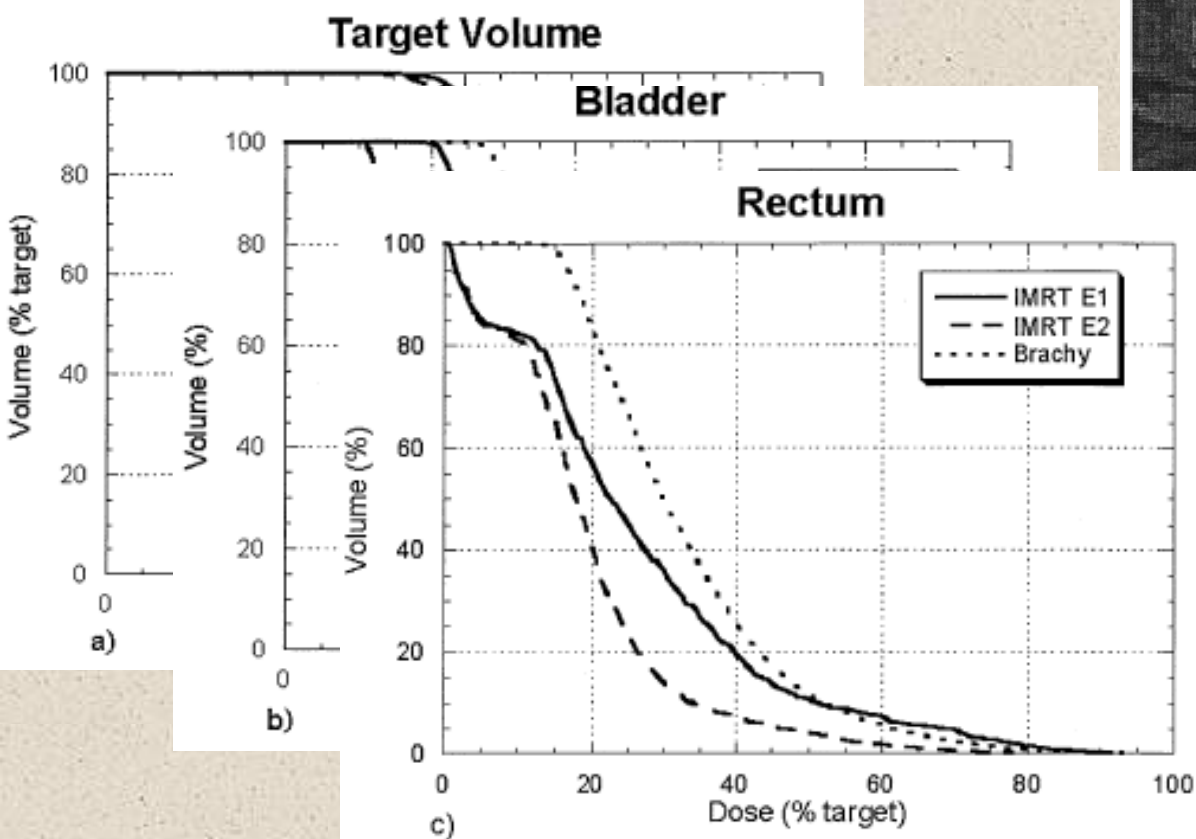


Fig. 1. Isodose distributions for treatment plans similar to those shown in Fig. 2. Doses are shown as percentages of

APPLICATOR-GUIDED INTENSITY-MODULATED RADIATION THERAPY

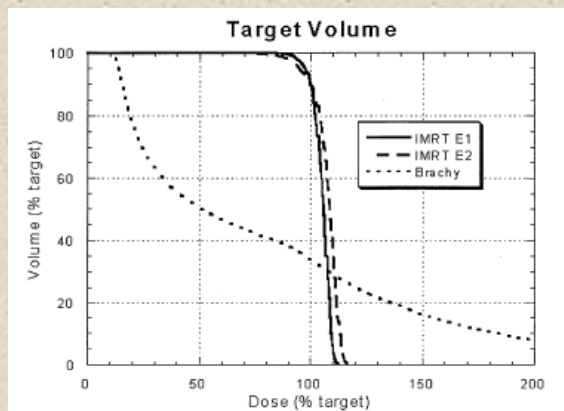
DANIEL A. LOW, PH.D., PERRY W. GRIGSBY, M.D., JAMES F. DEMPSEY, PH.D., SASA MUTIC, M.S.,
JEFFREY F. WILLIAMSON, PH.D., JERRY MARKMAN, D.Sc.,¹ K. S. CLIFFORD CHAO, M.D.,
ERIC E. KLEIN, M.S., AND JAMES A. PURDY, PH.D.

Int. J. Radiation Oncology Biol. Phys., Vol. 52, No. 5, pp. 1400-1406, 2002



APPLICATOR-GUIDED INTENSITY-MODULATED RADIATION THERAPY

DANIEL A. LOW, PH.D., PERRY W. GRIGSBY, M.D., JAMES F. DEMPSEY, PH.D., SASA MUTIC, M.S.,
JEFFREY F. WILLIAMSON, PH.D., JERRY MARKMAN, D.Sc.,¹ K. S. CLIFFORD CHAO, M.D.,
ERIC E. KLEIN, M.S., AND JAMES A. PURDY, PH.D.



Copertura target: vantaggio IMRT
tossicità: vantaggio IMRT

“patient repositioning will occur with the applicator substitute placed in the Vagina and uterus”

plans. The AGIMRT dose distributions provide an improved minimum dose to tumor, but are unable to deliver extremely high doses near the applicator positions like the brachytherapy treatment plans.

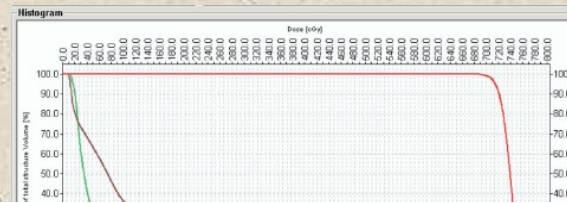
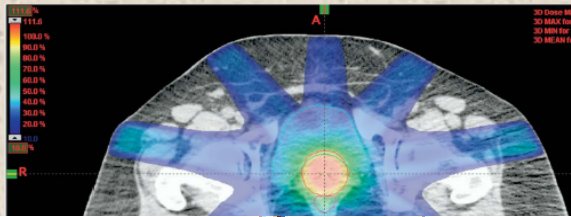
IMRT vs BT

Autore	N pts	Dose pelvi Gy	Gy/fr IMRT	Gy/fr BT	PTV margin IMRT	Target Copertura Dose (BED)		retto		Vescica	
						IMRT	BT	IMRT	BT	IMRT	BT
Roeske 2000	10	45	34/6	3DCRT 34/6	10 mm	3DCRT 79 Gy	79 Gy	3DCRT V50 62	93	3DCRT V50 75	95
Wahab 2004	10	30.6	57.6/2	39/6.5	Fletcher 5 mm	90% 83.2 Gy	82%	2.2% <40 Gy	4.1%	61% <45Gy	16.6%
Assenholt 2008	6	45	28/4	28/4	HR-CTV 3 mm	98%	74%	300 V60	550	82 Gy	90
Shwetha 2011	10	nd	30/5	30/5		103%	104%	77%	87%	81%	88%

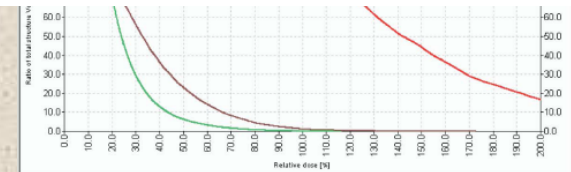
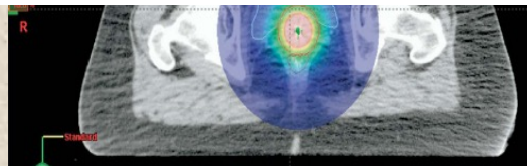
IMRT vs BT

Post-isterectomy

Autore	N pts	Dose pelvi Gy	Gy/fr IMRT	Gy/fr BT	PTV margin IMRT	Target		retto		Vescica	
						IMRT	BT	IMRT	BT	IMRT	BT
Aydogan 2006	10	45	21/3	21/3	CTV 5 mm	108%	241%	72%	84%	66%	74%



Conclusion: Our dosimetric analysis suggests that when used in conjunction with a suitable immobilization system, IMRT may provide an alternative to HDR brachytherapy in women with early endometrial cancer after hysterectomy. However, more studies are needed to evaluate the clinical merit of the IMRT in these patients.



**SIMULTANEOUS INTEGRATED INTENSITY-MODULATED RADIOTHERAPY
BOOST FOR LOCALLY ADVANCED GYNECOLOGICAL CANCER:
RADIOBIOLOGICAL AND DOSIMETRIC CONSIDERATIONS**

MARIANA GUERRERO, PH.D.,* X. ALLEN LI, PH.D.,[†] LIJUN MA, PH.D.,* JEANETTE LINDER, M.D.,*
CHAD DEYOUNG, M.D.,* AND BETH ERICKSON, M.D.[†]

Int. J. Radiation Oncology Biol. Phys., Vol. 62, No. 3, pp. 933-939, 2005

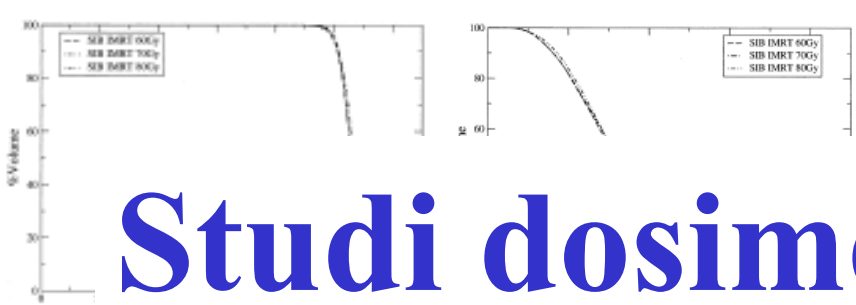
treatment	Dose pelvi		Dose boost		Dose tumore		BED (Gy10) tumore	BED (Gy3) OAR
WPI+IMRT	45	1.8 x25	17.5	2.5x7	62.5		68.7	72.0
WPI+HDR	45	1.8 x25	30	6x5	75		88	94.5
SIB IMRT	45	1.8 x25	31.4	1.26x25	76.4	3.06X25	88.1	91.6

SIMULTANEOUS INTEGRATED INTENSITY-MODULATED RADIOTHERAPY BOOST FOR LOCALLY ADVANCED GYNECOLOGICAL CANCER: RADIOBIOLOGICAL AND DOSIMETRIC CONSIDERATIONS

MARIANA GUERRERO, PH.D.,* X. ALLEN LI, PH.D.,† LIJUN MA, PH.D.,* JEANETTE LINDER, M.D.,*
CHAD DEYOUNG, M.D.,* AND BETH ERICKSON, M.D.†

Int. J. Radiation Oncology Biol. Phys., Vol. 62, No. 3, pp. 933-939, 2005

25 frazioni 45 Gy pelvi SIB 60 Gy cervice
70 Gy cervice
80 Gy cervice

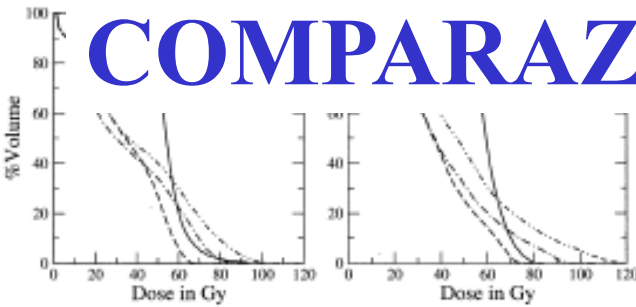


“A dose of 60 to 70 Gy can be safely
for an SIB IMRT schedule”

Studi dosimetrici

GTV

bowel



rectum

bladder

COMPARAZIONE CON BT NO High-tech

80 Gy: increased toxicity for
rectum and vescica

IMAGE-GUIDED RADIOTHERAPY FOR CERVIX CANCER: HIGH-TECH EXTERNAL BEAM THERAPY VERSUS HIGH-TECH BRACHYTHERAPY

DIETMAR GEORG, PH.D., CHRISTIAN KIRISITS, PH.D., MARTIN HILLBRAND, M.SC.,
JOHANNES DIMOPOULOS, M.D., AND RICHARD PÖTTER, M.D., PH.D.

Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 4, pp. 1272–1278, 2008

Pelvi IMRT 45 Gy
boost 7 Gy x4

IMRT vs IG-HDR BT

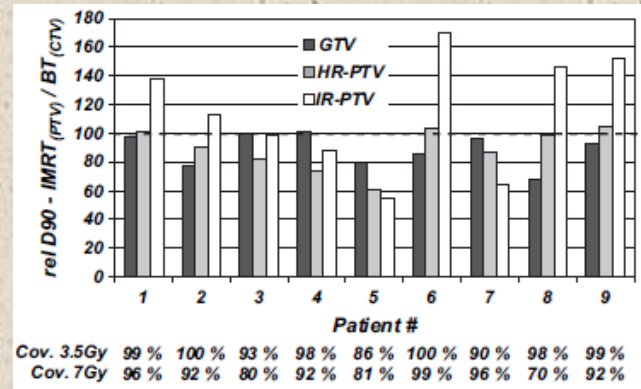
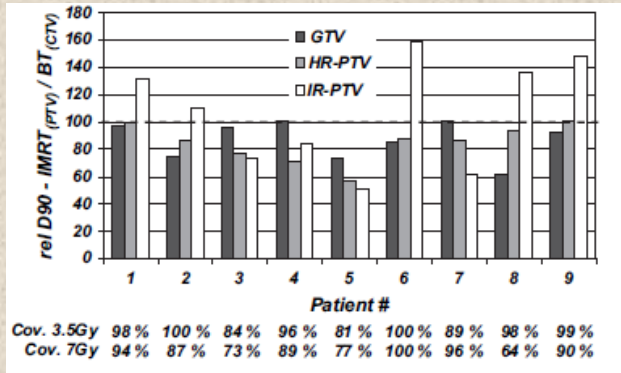
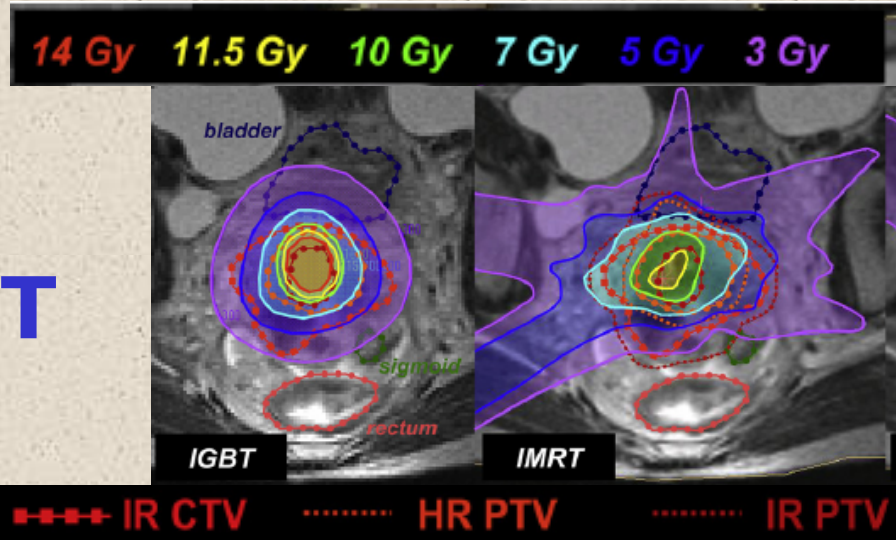


IMAGE-GUIDED RADIOTHERAPY FOR CERVIX CANCER: HIGH-TECH EXTERNAL BEAM THERAPY VERSUS HIGH-TECH BRACHYTHERAPY

DIETMAR GEORG, PH.D., CHRISTIAN KIRISITS, PH.D., MARTIN HILLBRAND, M.SC.,
JOHANNES DIMOPOULOS, M.D., AND RICHARD PÖTTER, M.D., PH.D.

Dose level	$D_{\text{tot,iso}}$ (Gy)	IMRT (%)		
		Mean \pm SD	Minimum	Maximum
5-mm margin				
3 Gy	58	215 \pm 34	151	252
3.5 Gy	62	200 \pm 34	148	249
5 Gy	75	153 \pm 36	115	207
7 Gy	99	94 \pm 22	66	130
3-mm margin				
3 Gy	58	208 \pm 38	144	264
3.5 Gy	62	192 \pm 38	142	230

Conclusion: For benchmarking high-tech EBT, high-tech BT techniques have to be used. For cervix cancer boost treatments, both IMRT and IMPT seem to be inferior to advanced BT. © 2008 Elsevier Inc.

TABLE 3. Average, minimum, and maximum volumes (in cubic centimeters) receiving fractional doses ≥ 3 Gy

$V_{3\text{Gy}}$	Mean \pm SD	Minimum	Maximum	$\geq 600 \text{ cm}^3$	$\leq 450 \text{ cm}^3$	<i>p</i>
BT	348 \pm 109	206	537	0	7	
IMRT 5 mm	752 \pm 294	519	1320	6	0	0.003
IMRT 3 mm	721 \pm 279	515	1221	4	0	0.004
IMPT 5 mm	522 \pm 130	347	741	2	3	0.007
IMPT 3 mm	469 \pm 109	323	666	1	4	0.032

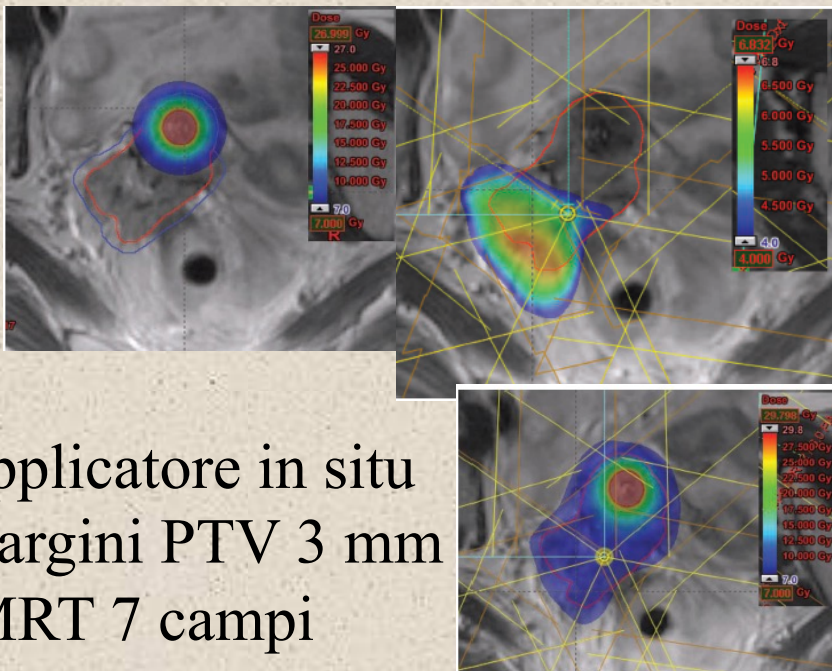
A dose planning study on applicator guided stereotactic IMRT boost in combination with 3D MRI based brachytherapy in locally advanced cervical cancer

Acta Oncologica, 2008; 47: 1337–1343

MARIANNE S. ASSENHOLT¹, JØRGEN B. PETERSEN¹, SØREN K. NIELSEN¹, JACOB C. LINDEGAARD² & KARI TANDERUP²

45 Gy pelvi IMRT seguita da HDR-BT gec-estro 7 Gyx4

IC-BT combined IMRT



	IC/IS-BT	IC-BT+IMRT	p-value
V100%	95% [78%–99%]	96% [69%–99%]	0.94
D100	62Gy [53–71]	69Gy [68–76]	0.11
D90	90Gy [70–97]	87Gy [79–89]	0.94
V60Gy	330cc [200–476]	399cc [312–570]	<0.01
Rectum, D2cc	75Gy [69–75]	75Gy [70–75]	0.25
Sigmoid, D2cc	71Gy [53–75]	72Gy [66–75]	0.12
Bladder, D2cc	79Gy [63–90]	87Gy [59–90]	0.29

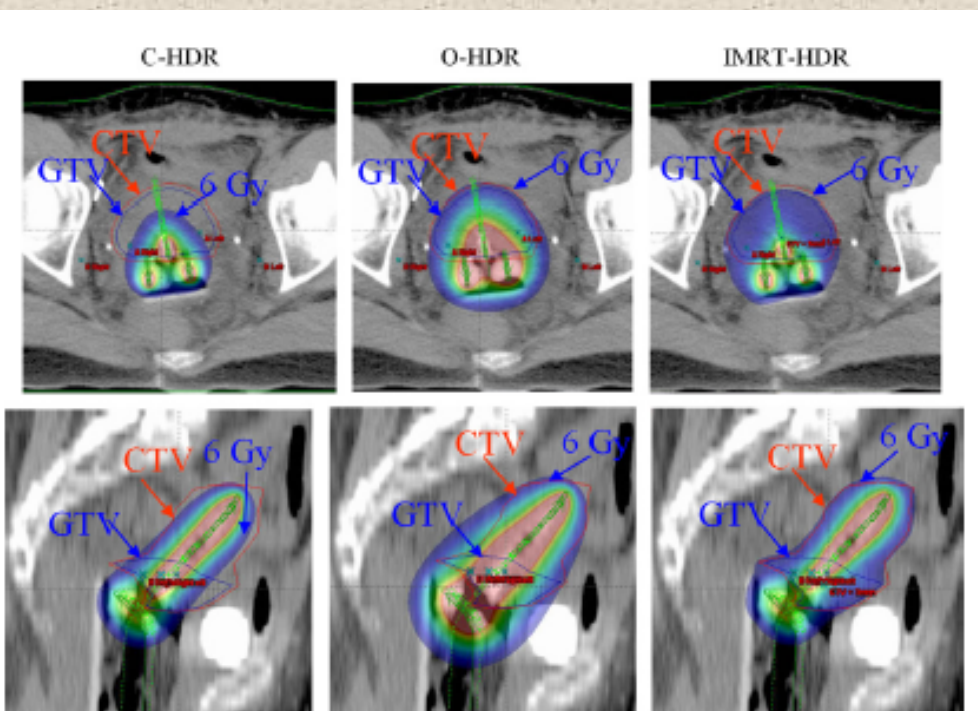
Applicatore in situ
 Margini PTV 3 mm
 IMRT 7 campi

favourable technique. *Conclusion.* It is technically possible to create dose plans that combine image guided BT and IMRT. In this study the dose coverage could be significantly increased by adding IS-BT or IMRT boost to the intracavitary dose. Using IMRT alone for boost cannot be advocated since this results in a significant increase of the volume irradiated to 60Gy.

CONVENTIONAL HIGH-DOSE-RATE BRACHYTHERTHAPY WITH CONCOMITANT COMPLEMENTARY IMRT BOOST: A NOVEL APPROACH FOR IMPROVING CERVICAL TUMOR DOSE COVERAGE

JUN DUAN, PH.D.,* ROBERT Y. KIM, M.D.,* SHAABAN ELASSAL, M.D.,* HUI-YI LIN, PH.D.,[†]
AND SUI SHEN, PH.D.*

Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 3, pp. 765-771, 2008



		Minimum	Maximum	Median
GTV ⁺ Coverage	C-HDR	32.2	81.6	51.2
	O-HDR	95.3	99.8	98.4
	IMRT-HDR	54.3	97.2	91.7
V ₉₅	C-HDR	34.3	84.3	55.1
	O-HDR	96.9	99.4	98.7
	IMRT-HDR	68.9	100.0	96.4
CTV Coverage	C-HDR	25.7	91.0	38.9
	O-HDR	66.6	96.6	89.5
	IMRT-HDR	64.1	99.7	93.2
V ₉₅	C-HDR	27.7	94.4	39.3
	O-HDR	66.3	97.5	90.4
	IMRT-HDR	77.4	100.0	98.6

	D ₂	Technique	Minimum	Maximum	Median
Rectum	C-HDR		53.1	83.0	58.9
	O-HDR		86.9	389.0	119.4
	IMRT-HDR		63.4	88.0	68.8
Bladder	C-HDR		59.1	162.2	77.2
	O-HDR		118.6	333.0	222.5
	IMRT-HDR		64.2	86.9	72.8

Conclusion: Compared with C-HDR and O-HDR, concomitant IMRT boost complementary to C-HDR not only provided excellent CTV coverage, but also maintained reasonably low doses to the OARs. © 2008 Elsevier Inc.

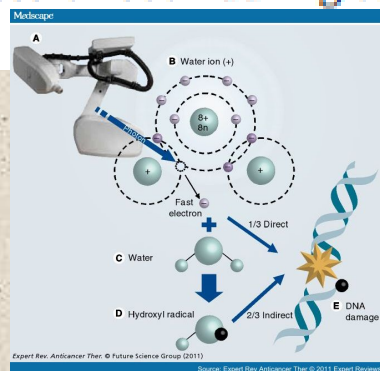
Stereotactic body radiotherapy (SBRT): Technological innovation and application in gynecologic oncology

Daniel S. Higginson^{a,*}, David E. Morris^a, Ellen L. Jones^a, Daniel Clarke-Pearson^b, Mahesh A. Varia^a

Gynecologic Oncology 120 (2011) 404–412

SBRT in gynecologic oncology

To date, SBRT has been used for gynecologic malignancies in the treatment of macroscopic pelvic and periaortic lymph nodes and oligometastatic disease. Potentially it could be used as a substitute for brachytherapy for some patients if brachytherapy is anatomically or dosimetrically unfavorable. Image guided therapy using cone-beam CT or fiducial tracking is highly advantageous for gynecologic malignancies to account for the significant degree of uterine movement due to bladder and rectum filling/emptying [7,21] and because of the 45–60% tumor regression seen during conventional RT (before SBRT boosts) [7,21,22].



Stereotactic body radiotherapy (SBRT): Technological innovation and application in gynecologic oncology

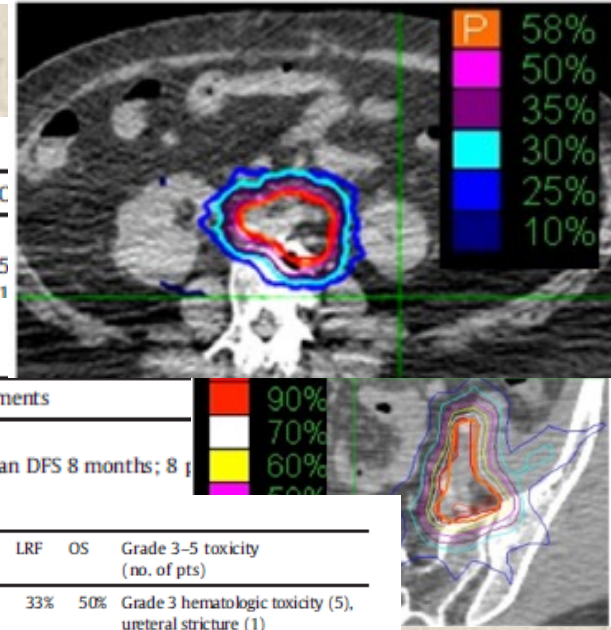
Daniel S. Higginson^{a,*}, David E. Morris^a, Ellen L. Jones^a, Daniel Clarke-Pearson^b, Mahesh A. Varia^a

Table 1
Salvage radiotherapy for isolated periaortic node recurrences.

First author	Patients	Final dose to PAN (Gy)	Chemotherapy	N	F/u	LRF	C
<i>Conventional RT</i>							
Chou [24]	Cervical	45	Concurrent cisplatin.	14	5 y	-	5
Sinh [25]	Cervical	45-50.4	Concurrent navelbine, irinotecan	7	5 y	-	1

Table 2
The treatment of oligometastatic disease in gynecologic malignancies.

Author	Patients	N	F/u (y)	5 y OS	Toxicity	Comments		
<i>Lung resections</i>								
Clavero [63]	Endometrial (60), cervical (7), ovarian (2), vaginal (1)	70	3	47%	1 death, 26% complication rate	Median DFS 8 months; 8		
<i>The use of SBRT for gynecologic malignancies.</i>								
Author	Histology (no. of pts)	Sites treated	SBRT dose Gy/fx (no. of pts)	N	F/U (m)	LRF	OS	Grade 3-5 toxicity (no. of pts)
Choi [29]	Cervical (28), endometrial (2)	Periaortic node recurrences	33-45/3 ^a	30	48	33%	50%	Grade 3 hematologic toxicity (5), ureteral stricture (1)
Deodato [72]	Cervical (4), endometrial (3), ovarian (4)	Pelvic, mediastinal, inguinal lymph nodes; cervix/vagina; liver, adrenal mets.	20-30/4-6	11	19	33	64	None
Gucken-berger [78]	Cervical (12), endometrial (7)	Pelvic recurrences after prior surgery (12), surgery and RT (6), or RT alone (1)	15/3(16), 30/3(2), 28/4 (1) ^b	19	22	29	34	Grade 4 intestino-vaginal fistula (2), grade 4 small bowel ileus (1), grade 3 urinary frequency (1), Grade 3 fatigue(1)
Kunos [80]	Cervical (1), endometrial (1), ovarian (3)	Proximal vaginal recurrences	15-24/3 ^c	5	9	20	80	
Kunos [79]	Vulvar	Labial lesions (3) and pelvic nodes (1)	24/3 ^d	3	3	100	100	Vesicovaginal fistula (1)
Molla [77]	Cervical (7), Endometrial (9)	Final adjuvant boost to upper vagina, parametria after prior surgery (14) or for local relapse (2) after surgery or RT	14/2(12), 20/5(3), 40/10(1).	16	13	6	100	Grade 3 rectal bleeding (1)
<i>Liver resections</i>								
Lim [66]	Ovarian							
Chi [68]	Cervical (2), end fallopian tube (1)							



SBRT: stereotactic body radiotherapy; PAN: periaortic node; LRF: local relapse-free; OS: overall survival; F/U: follow-up; Gy: gray; fx: fraction; N: number of patients; m: months; LRF: local relapse-free; OS: overall survival; F/U: follow-up; Gy: gray; fx: fraction; N: number of patients; m: months.

Autore	Pts (n)	Disease type	Radiosurgery technique	PTV Margin mm	Dose range	Toxicity	SBRT results
Kunos et al. (2008)	3	Vulva	Robotic	none	8 Gy × 3	3 grade 2 skin	1 year target control; 0 out of 3 (0%), non-SBRT target geometric miss in 3 patients
Kunos et al. (2009)	3	1 cervix, 2 endometrial, 2 ovary	Robotic	5	5–8 Gy × 3	3 grade 2 diarrhea, 1 grade 2 urgency	2 year target control; 5 out of 5 (100%)
Molla et al. (2005)	16	7 cervix, 9 endometrial	Dynamic arc or IMRT	10	5–8 Gy × 3	1 grade 3 rectal bleed	1 year target control; 15 out of 16 (94%)
Jorcano et al. (2010)	26	9 cervix, 17 endometrial	Dynamic arc or IMRT	10	7 Gy × 2	23% grade 2 urinary, 35% grade 2 gastrointestinal	3 year target control; 25 out of 26 (96%)
Guckenberger et al. (2010)	19	12 cervix, 7 endometrial	IMRT	5	5 Gy × 3	Grade 4 ileus (1), grade 4 enterovaginal fistula (2), grade 2 diarrhea (2), grade 3 dysuria (1)	2 year target control; 16 out of 19 (81%)
Deodato (2009)	11	4 cervical, 3 endometrial 4 ovarian	ESRT	10	4-6 Gy x 4-5	None G3	2 year target control: 2 out of 11 (89%)
Higginson (2011)	5	1 endometrial 2 vaginal 1cervix 1 bladder	Robots	none	5 Gy x 5	G3 rectal bleeding G2 acute cystitis	1 year 80%

FRACTIONATED STEREOTACTIC RADIOTHERAPY BOOST FOR GYNECOLOGIC TUMORS: AN ALTERNATIVE TO BRACHYTHERAPY?

MERITXELL MOLLA, M.D.,* LLUÍS ESCUDE, D.Sc.,* PHILIPPE NOUET, D.Sc.,† YOURI POPOWSKI, D.Sc.,†
ALBERTO HIDALGO, M.D.,‡ MICHEL ROUZAUD, D.Sc.,† DOLORES LINERO, D.Sc.,* AND
RAYMOND MIRALBELL, M.D.*†

Int. J. Radiation Oncology Biol. Phys., Vol. 62, No. 1, pp. 118–124, 2005

45-50.4 pelvi
Boost su fondo vaginale, utero-parametri
residuo o recidiva

CTV espanso di 6-10 mm= PTV

12 IMRT isocentro singolo 5-15 campi

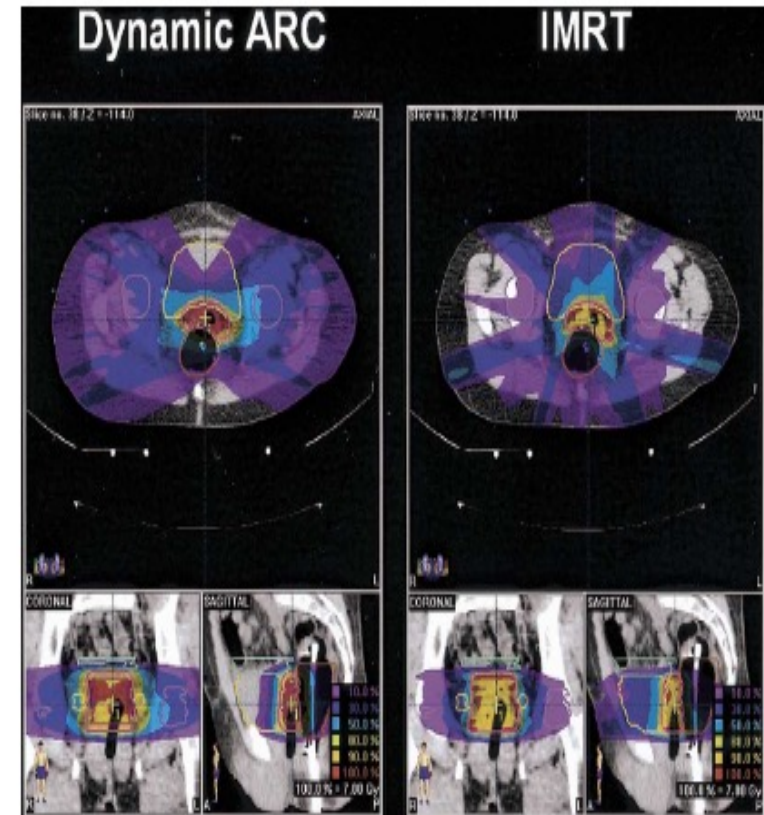
2 IMRT 2 isocentri 8-12 campi

1 tecnica con arco dinamico

12 postoperatorio 7 Gy x 2 ogni 4-7 giorni

3 radicale 4 Gy x 5 2 vv/settimana

1 re-irradiazione 2 Gy x 8 5 day/week 4 Gy x 10 2 vv/week



FRACTIONATED STEREOTACTIC RADIOTHERAPY BOOST FOR GYNECOLOGIC TUMORS: AN ALTERNATIVE TO BRACHYTHERAPY?

MERITXELL MOLLA, M.D.,* LLUÍS ESCUDE, D.Sc.,* PHILIPPE NOUET, D.Sc.,† YOURI POPOWSKI, D.Sc.,†
ALBERTO HIDALGO, M.D.,‡ MICHEL ROUZAUD, D.Sc.,† DOLORES LINERO, D.Sc.,* AND
RAYMOND MIRALBELL, M.D.*†

Follow-up 12.6 mesi (range 6-26)

1 recidiva centrale dopo 12 mesi in pz postoperatoria

Table 2. Radiation tolerance

Site and grade	Acute	Late
Sexual		
Grade 0	10	9
Grade 1	4	7
Grade 2	2	0
Grade 3	0	0
Urinary		
Grade 0	12	16
Grade 1	1	0
Grade 2	3	0
Grade 3	0	0
Rectum		
Grade 0	9	14
Grade 1	5	1
Grade 2	2	0
Grade 3	0	1

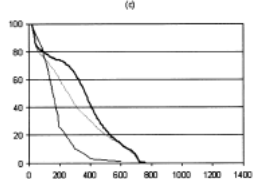
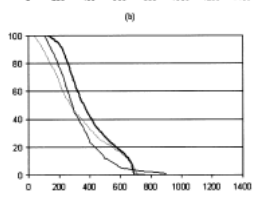
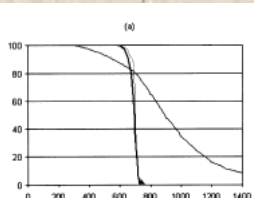
1/16 (6.25%)

FRACTIONATED STEREOTACTIC RADIOTHERAPY BOOST FOR GYNECOLOGIC TUMORS: AN ALTERNATIVE TO BRACHYTHERAPY?

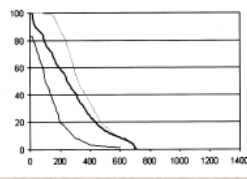
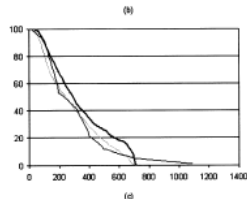
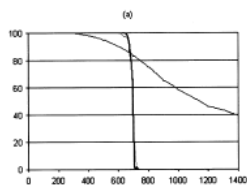
MERITXELL MOLLA, M.D.,* LLUÍS ESCUDE, D.Sc.,* PHILIPPE NOUET, D.Sc.,† YOURI POPOWSKI, D.Sc.,†
ALBERTO HIDALGO, M.D.,‡ MICHEL ROUZAUD, D.Sc.,† DOLORES LINERO, D.Sc.,* AND
RAYMOND MIRALBELL, M.D.*†

SRT (IMRT e arco-dinamico)
CTV 3 cm di vagina e 5 mm di mucosa vaginale
PTV=CTV+6-10mm
arco-dinamico
singolo isocentro 1 arco (240°-120°)
2 archi (240°-320° e 40°-120°)
IMRT singolo isocentro e 7 campi co-planari

HDR-BT 2D
7 Gy x2



— IMRT
- - Arc
... BT



— IMRT
- - Arc
... BT

SRT

Migliore omogeneità di dose
Riduzione della dose max al retto

BT

Vantaggiosa per la vescica

Hypofractionated extracranial stereotactic radiotherapy boost for gynecologic tumors: a promising alternative to High-dose Rate brachytherapy

Jorcano, Technol Can Res Treat 2010

26 pts 45-50.4 pelvi

7 Gyx2 Boost su CTV=3 cm da apice vagina

PTV=CTV + 6-10 mm, dynamic arc

IR-guided system

Endorectal probe, no filler bladder control

Alprazolam x os

Median follow-up

47 mesi (range 4-77)

late GI G2-3

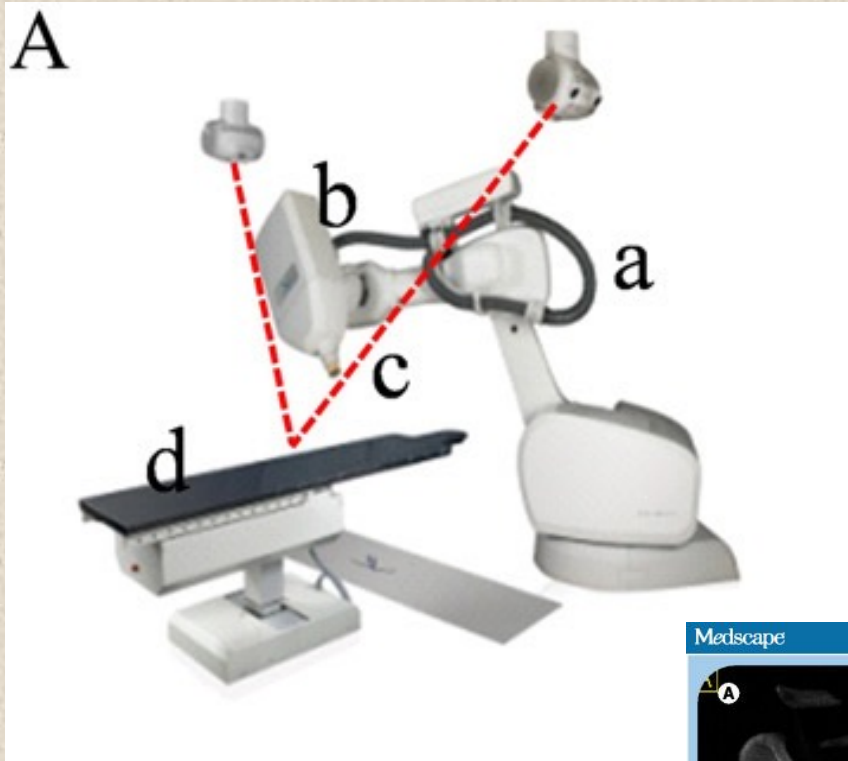
Late sexual G2-3

3 pts (11%)

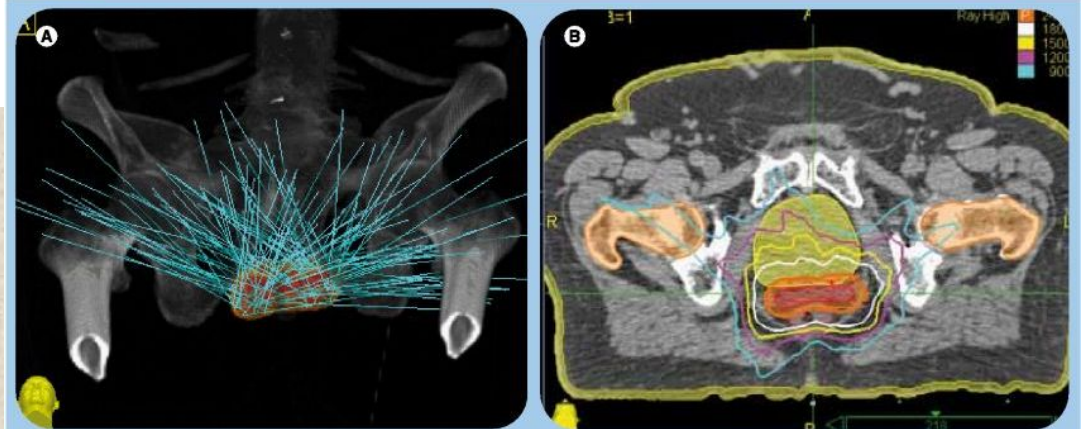
5 pts (19%)

FFS 3-yrs 96%

OS 3-yrs 95%



Medscape



Source: Expert Rev Anticancer Ther © 2011 Expert Reviews Ltd

Stereotactic Body Radiosurgery for Pelvic Relapse of Gynecologic Malignancies

Charles Kunos, M.D., Ph.D.^{1*}

Technology in Cancer Research and Treatment

ISSN 1533-0346

Volume 8, Number 5, October 2009

Patient	Disease	Treatment Volume	Imaging	Prior RT Dose	Prescription Dose (Isodose Line)	BED @ 100% IDL ($\alpha/\beta = 10$)	Target Lesion Control	Relapse
1	endometrial cancer, relapse of proximal vagina	20.8 cm ³	CT	45 Gy / 25 fx 21 Gy / 3 fx	5 Gy x 3 fx (70% IDL)	32.1 GY	CR	pulmonary metastases @ 5 months, no pelvic disease @ 19 months
2	cervix cancer, relapse of proximal vagina	217.5 cm ³	CT	45 Gy / 25 fx 30 Gy / 1 fx	6.5 Gy x 3 fx (70% IDL)	46 Gy	PR	non-targetted persistent left flank disease, no pelvic disease @ 4 months
3	ovarian cancer, relapse of proximal vagina	18.5 cm ³	CT	10 Gy x 1 fx	8 Gy x 3 fx (75% IDL)	57.6 Gy	CR	non-targetted distal vagina @ 9 months
4	ovarian cancer, relapse of proximal vagina	20.0 cm ³	CT/MRI	45 Gy / 25 fx	6 Gy x 3 fx (80% IDL)	36 Gy	CR	none @ 10 months
5	ovarian cancer, relapse of proximal vagina	190.8 cm ³	CT/MRI	10 Gy / 1 fx	8 Gy x 3 fx (70% IDL)	61.7 Gy	PR	none @ 6 months

4-6 soft tissue fiducial markers

PTV: GTV + 5 mm margin 18.5cc-217cc

Prescrizione 70%-80%

Overall treatment time 72-104 min

Stereotactic Body Radiosurgery for Pelvic Relapse of Gynecologic Malignancies

Charles Kunos, M.D., Ph.D.^{1*}

Technology in Cancer Research and Treatment

ISSN 1533-0346

Volume 8, Number 5, October 2009

Table II

Acute toxicity assessment, according to the National Cancer Institute's Common Terminology Criteria for Adverse Events v3.0.

CTCAE toxicity	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Blood / Bone Marrow	-	-	1 (anemia)	-	-
Cardiac	-	-	-	-	-
Coagulation	-	-	-	-	-
Constitutional symptoms	3 (fatigue)	-	-	-	-
Death	-	-	-	-	-
Dermatology / Skin	-	-	-	-	-
Endocrine	-	-	-	-	-
Gastrointestinal	-	2 (obstruction) 2 (diarrhea)	2 (tenesmus)	1 (diarrhea)	2 (diarrhea)
Hemorrhage / Bleeding	-	-	1 (rectal)	-	-
Hepatobiliary / Pancreas	-	-	-	-	-
Infection	2 (urinary)	-	-	-	-
Lymphatics	-	1 (limb edema)	-	-	-
Musculoskeletal / Soft tissue	-	-	-	-	-
Neurology	-	-	-	-	-
Pain	-	-	-	1 (pain)	2 (pain)
Pulmonary / Upper respiratory	-	-	-	-	-
Renal / GU	1 (incontinence)	2 (obstruction)	2 (urgency)	1 (hesitancy)	-
Secondary Malignancy	-	-	-	-	-
Sexual / Reproductive function	-	-	-	-	-
Vascular	-	2 (thrombosis)	-	-	-

4-6 soft tissue fiducial markers

PTV: GTV + 5 mm margin 18.5cc-217cc

Prescrizione 70%-80%

Overall treatment time 72-104 min

Stereotactic body radiotherapy (SBRT): Technological innovation and application in gynecologic oncology

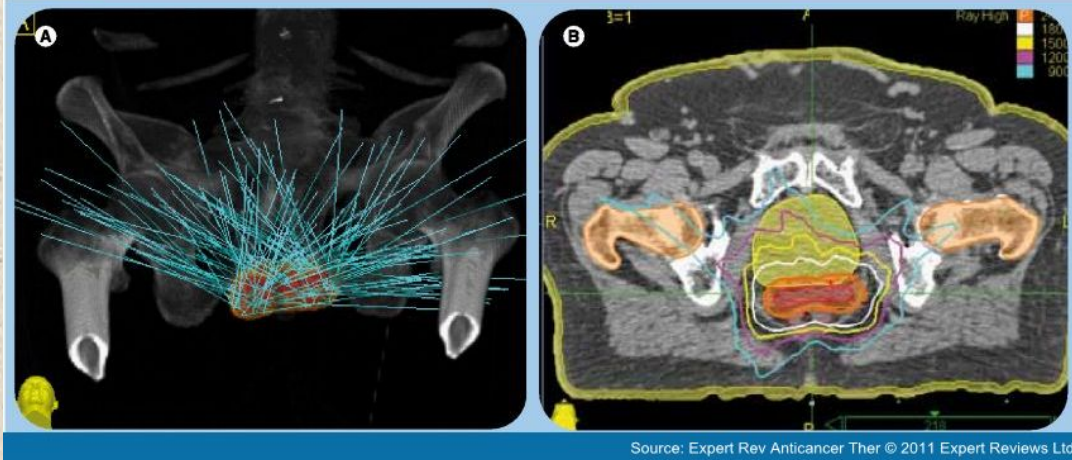
Daniel S. Higginson^{a,*}, David E. Morris^a, Ellen L. Jones^a, Daniel Clarke-Pearson^b, Mahesh A. Varia^a

Gynecologic Oncology 120 (2011) 404–412

SBRT used for gynecologic malignancies or sites of disease at the University of North Carolina.

Pt. no	Age	Histology	Clinical setting	DFI (m.)	RT (Gy)	SBRT (Gy/fx)	F/u (m.)	LR control ^P	Systemic failures ^b	Status	Toxicity ^c
<i>Substitute for brachytherapy</i>											
12	89	Endometrial ^d	Medically inoperable, could not tolerate brachytherapy	-	48.8	20/5	8	-	Unknown	Dead	Late grade 3 rectal bleeding
13	67	Vaginal ^f	Periurethral location	-	45	25/5	22	-	Lung mets. @17 m.	DOD	Acute grade 2 radiation cystitis
14	62	Vaginal ^f	Prior cervical ca. in 1981. Now upper vaginal cuff disease.	-	40	25/5	7	@5 months	-	DOD	None
15	77	Urothelial carcinoma of the bladder	Recurrent disease at vaginal apex after prior cystectomy	6	45	16/4	12	-	-	NED	None
16	51	Cervix ^e	Recurrent disease within vaginal cuff after prior chemoradiation	34	-	25/5	10	-	Liver mets. @2 m.	DOD	None

“In our practice, we have used Cyberknife SBRT when patients have no reasonable option to receive brachytherapy”



Stereotactic body radiotherapy (SBRT): Technological innovation and application in gynecologic oncology

Daniel S. Higginson^{a,*}, David E. Morris^a, Ellen L. Jones^a, Daniel Clarke-Pearson^b, Mahesh A. Varia^a

Gynecologic Oncology 120 (2011) 404–412

“As an alternative option if brachytherapy (either intracavitary or interstitial) is impossible, SBRT may be substituted for brachytherapy, much like 3D conformal EBRT and IMRT”

geometric miss

Autore	Pts (n)	Disease type	Radiosurgery technique	CTV Margin mm	Dose range	Toxicity	SBRT results
Kunos et al. (2008)	3	Vulva	Robotic	none	8 Gy × 3	3 grade 2 skin	1 year target control; 0 out of 3 (0%), non-SBRT target geometric miss in 3 patients

Cyberknife Radiosurgery for Squamous Cell Carcinoma of Vulva After Prior Pelvic Radiation Therapy

Charles Kunos, MD, Ph.D.^{1,2}

Technology in Cancer Research and Treatment

ISSN 1533-0346

Volume 7, Number 5, October 2008

©Adaptive Press (2008)

“While targeting accuracy through the course of treatment was addressed by continuous monitoring of digitally reconstructed orthogonal radiographs to confirm 3-D orientation of implanted fiducial markers”

...suggests that geographic miss due to insufficient irradiated margin..

geometric miss Therefore , we suggest expanding the tumor target dimensions by 0.5 cm to create a PTV to assist in sterilizing occult microscopic disease surrounding the GTV

PROTONI

LONG-TERM RESULTS OF PROTON BEAM THERAPY FOR CARCINOMA OF THE UTERINE CERVIX

KENJI KAGEL, M.D.,*† KOICHI TOKUUYE, M.D.,*† TOSHIYUKI OKUMURA, M.D.,‡
KIYOSHI OHARA, M.D.,† YOSHIYUKI SHIOYAMA, M.D.,*†§ SHINJI SUGAHARA, M.D.,† AND
YASUYUKI AKINE, M.D.*†

Int. J. Radiation Oncology Biol. Phys., Vol. 55, No. 5, pp. 1265-1271, 2003

25 pts stadio IIB-IVA

Pelvi fotoni 50.4 Gy schermo centrale a 25 Gy

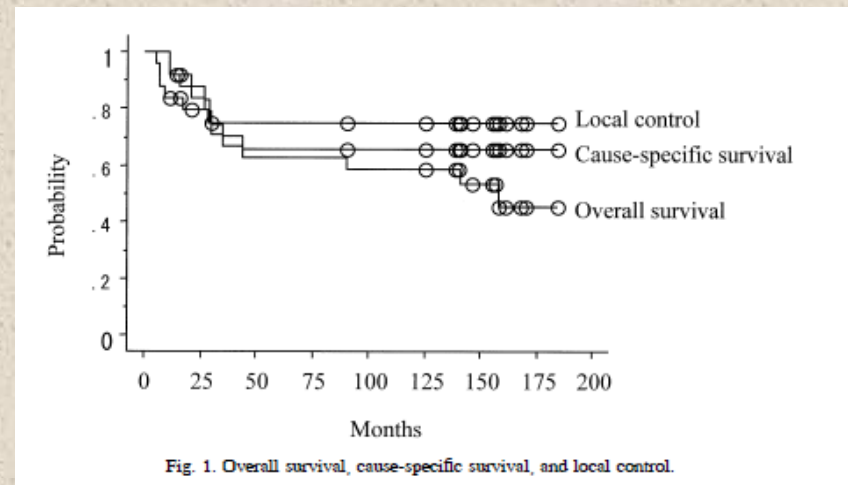
Boost Protoni

CTV= GTV+5-10 mm di margine

2.5-4 Gy/settimana

dose totale 86 Gy (71-101 Gy)

Markers metallici per treatment set-up

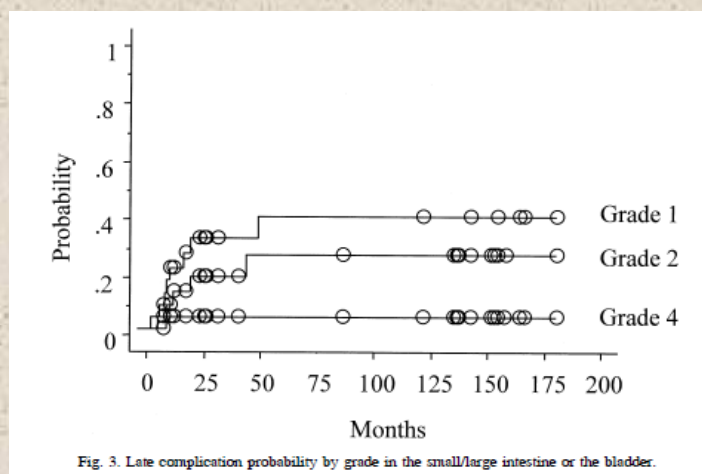


LONG-TERM RESULTS OF PROTON BEAM THERAPY FOR CARCINOMA OF THE UTERINE CERVIX

KENJI KAGEI, M.D.,*† KOICHI TOKUYE, M.D.,*† TOSHIYUKI OKUMURA, M.D.,‡
KIYOSHI OHARA, M.D.,† YOSHIYUKI SHIOYAMA, M.D.,*†§ SHINJI SUGAHARA, M.D.,† AND
YASUYUKI AKINE, M.D.*†

Table 3. Grades 2-5 late complications in the small/large intestine or the bladder according to patient or tumor-related characteristics

Factor	Patients (n)	Grades 2-5 late complication	
		% at 5 yr	p value
Age			
<63 yr	12	29	
>63 yr	13	30	<i>p</i> = 0.57
Stage			
Stage IIB	9	48	
Stage IIB/IVA	16	13	<i>p</i> = 0.20
Combined equivalent dose (2 Gy, $\alpha/\beta = 3$)*			
<102 Gy	12	11	
>102 Gy	13	49	<i>p</i> = 0.06
Proton equivalent dose (2 Gy, $\alpha/\beta = 3$)*			
<78 Gy	13	10	
>78 Gy	12	51	<i>p</i> = 0.040
Overall treatment time			
<63 days	12	34	
>63 days	13	24	<i>p</i> = 0.98



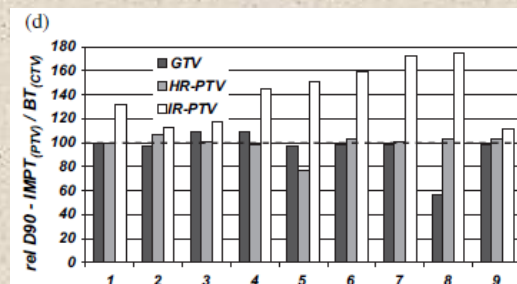
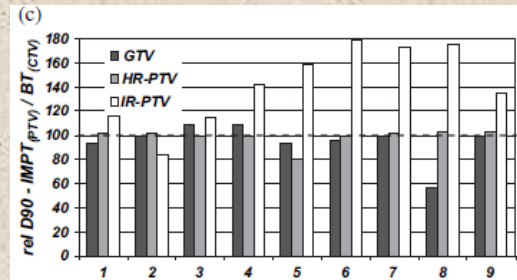
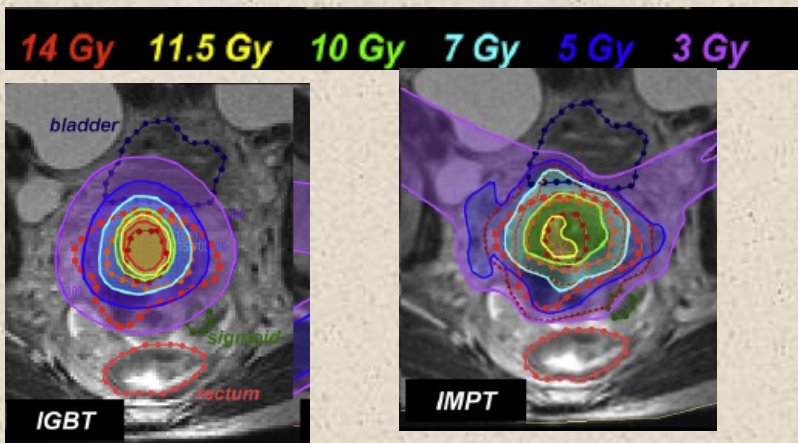
Actuarial rates of late complications for grades 1, 2, and 4 at 5 years were 43%, 26%, and 4%, respectively.

In conclusion, proton therapy is a good alternative to intracavitary irradiation in the treatment of cervical cancer. Local control rates, survival rates, and the incidence of severe late complication after proton therapy are comparable with those after standard therapy.

IMAGE-GUIDED RADIOTHERAPY FOR CERVIX CANCER: HIGH-TECH EXTERNAL BEAM THERAPY VERSUS HIGH-TECH BRACHYTHERAPY

DIETMAR GEORG, PH.D., CHRISTIAN KIRISITS, PH.D., MARTIN HILLBRAND, M.Sc.,
JOHANNES DIMOPOULOS, M.D., AND RICHARD PÖTTER, M.D., PH.D.

IG-HDRBT protoni



Dose level	$D_{\text{int, iso}}$ (Gy)	IMPT (%)		
		Mean \pm SD	Minimum	Maximum
5-mm margin				
3 Gy	58	155 \pm 33	113	210
3.5 Gy	62	153 \pm 37	97	213
5 Gy	75	158 \pm 52	73	245
7 Gy	99	119 \pm 34	82	179
3-mm margin				
3 Gy	58	140 \pm 31	105	205
3.5 Gy	62	137 \pm 31	100	207
5 Gy	75	145 \pm 45	82	229
7 Gy	99	103 \pm 20	71	136

**Copertura target= simile
dose a intestino > per IMPT**

Brachiterapia vs EBRT

Le sorgenti sono posizionate internamente, in stretta prossimità al tumore,

con indubbi vantaggi dosimetrici

con riduzione massima dell' interfraction e intrafraction movement

Dose distribution

Duplicating a tandem and ovoids distribution with intensity-modulated radiotherapy: a feasibility study

Harish K. Malhotra, JOURNAL OF APPLIED CLINICAL MEDICAL PHYSICS, VOLUME 8, NUMBER 3, SUMMER 2007

HDR BT 7 Gy x 5

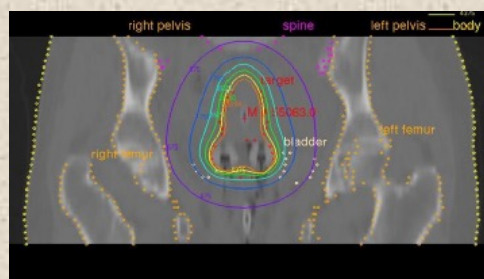
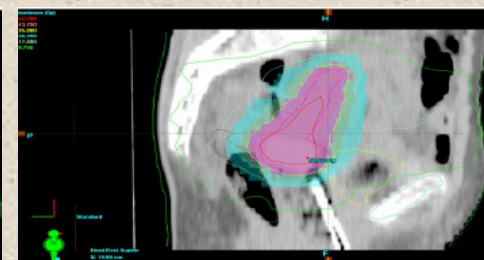
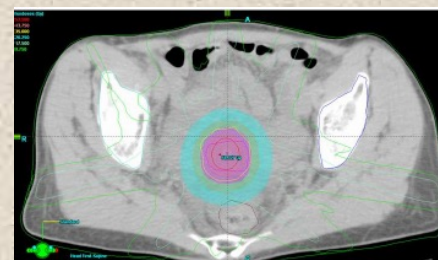
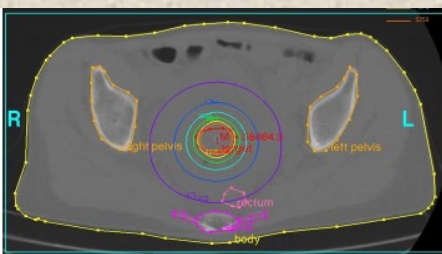
Point A

Isodosi 150%, 125%, 100%, 75%, 50% e 25%

IMRT 7 campi co-planari

Sliding windows

Target : isodose 100% BT



Dose distribution

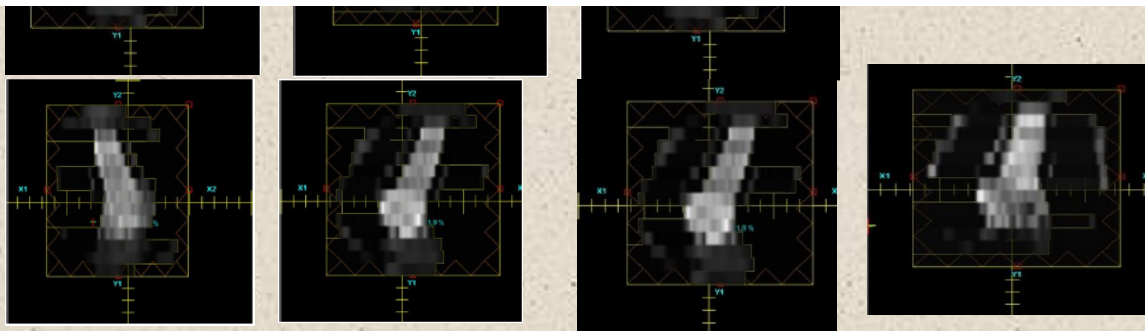
Duplicating a tandem and ovoids distribution with intensity-modulated radiotherapy: a feasibility study

Harish K. Malhotra, JOURNAL OF APPLIED CLINICAL MEDICAL PHYSICS, VOLUME 8, NUMBER 3, SUMMER 2007

110

V. CONCLUSIONS

Our preliminary results indicate that HDR distribution can be replicated using standard IMRT for all points lying close to point A, although the DVHs of rectum and bladder are not identical (a slightly higher dose is shown for those structures). Nevertheless, smaller facilities that lack HDR brachytherapy on site could offer equivalent IMRT treatments instead. The radiobiologic and patient positioning differences between the two techniques merit further consideration. However, the latter can be easily handled using standard pre-treatment imaging options available with treatment units having image-guided radiotherapy capabilities.



EBRT and Bt are fundamentally different with regard to need of margins that take set-up uncertainties into account

Any study that compares BT and EBRT should take into account that the dose should be delivered to a larger volume with EBRT (CTV + margins) than with BT (CTV)

Organ motion

Interfraction

intrafraction

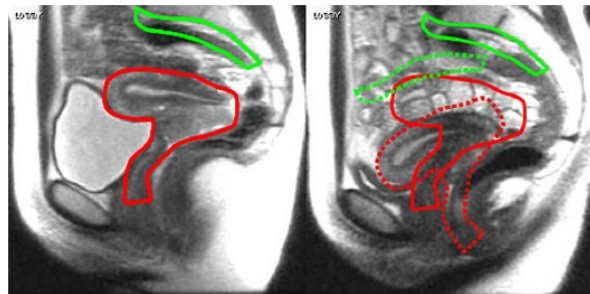
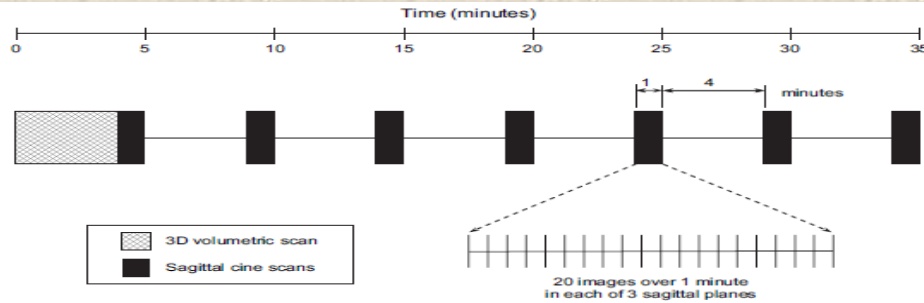


Fig. 7. Sagittal T₂-weighted MR images obtained 1 week apart from the same patient, demonstrating the marked difference between uterus and cervix positions, with altered bladder filling. Primary tumor CTV (red contour) and nodal CTV (green) contours overlaid. Solid lines represent targets at week 1, dashed lines represent the targets at week 2 if a direct translational shift is made to compensate for the change in the primary tumor CTV position. Nodal CTV and portions of tumor CTV in week 2 are missed.

INTER- AND INTRAFRACTIONAL TUMOR AND ORGAN MOVEMENT IN PATIENTS WITH CERVICAL CANCER UNDERGOING RADIOTHERAPY: A CINEMATIC-MRI POINT-OF-INTEREST STUDY

PHILIP CHAN, M.B.B.S.,*†† ROBERT DINNIWELL, M.D.,*†† MASOOM A. HAIDER, M.D.,§¶ YOUNG-BIN CHO, PH.D.,*† DAVID JAFFRAY, PH.D.,*† GINA LOCKWOOD, M.MATH.,|| WILFRED LEVIN, M.B.,*† LEE MANCHUL, M.D.,*† ANTHONY FYLES, M.D.,*†† AND MICHAEL MILOSEVIC, M.D.*††

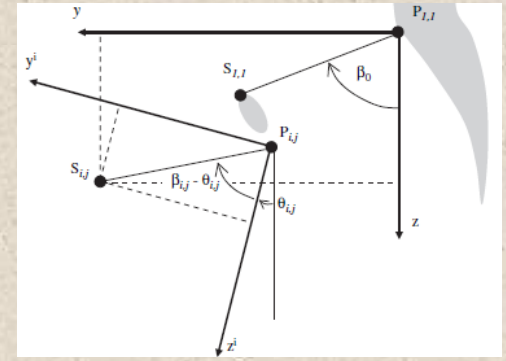
Radiation Oncology Biol. Phys., Vol. 70, No. 5, pp. 1507–1515, 2008



filling or other physiologic processes. The patients in this study were scanned each week for 31 min, similar to the time required to deliver high-precision pelvic RT. A small

Table 2. Interscan tumor and organ motion in patients with cervical cancer

Overall	Uterine fundus (F)		Uterine canal (C)		Cervical os (O)	
	AP	CC	AP	CC	AP	CC
Grand-mean (mm)	-4.6	7.8	-4.8	5.7	2.4	1.5
Mean-range (mm)	14.5	24.4	13.1	15.7	11.2	11.3
⁹⁰ PI (mm)						
Negative	-19.4	-21.8	-24.2	-11.0	-11.4	-11.9
Positive	10.7	37.6	15.2	21.9	16.6	15.2



Interfractional motion margin

Fundus 1-4 cm

Canal 1-2.5 cm

Os 1-1.5 cm

INTER- AND INTRAFRACTIONAL TUMOR AND ORGAN MOVEMENT IN PATIENTS WITH CERVICAL CANCER UNDERGOING RADIOTHERAPY: A CINEMATIC-MRI POINT-OF-INTEREST STUDY

PHILIP CHAN, M.B.B.S.,*†† ROBERT DINNIWELL, M.D.,*†† MASOOM A. HAIDER, M.D.,§¶ YOUNG-BIN CHO, PH.D.,*† DAVID JAFFRAY, PH.D.,*† GINA LOCKWOOD, M.MATH.,|| WILFRED LEVIN, M.B.,*† LEE MANCHUL, M.D.,*† ANTHONY FYLES, M.D.,*†† AND MICHAEL MILOSEVIC, M.D.*††

Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 5, pp. 1507–1515, 2008

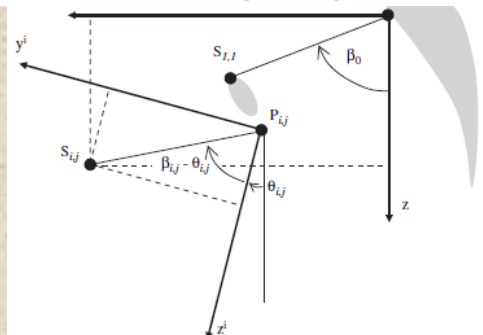
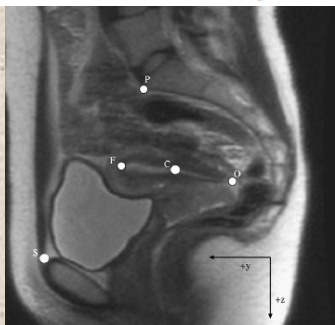


Table 2. Interscan tumor and organ motion in patients with cervical cancer

Overall	Uterine fundus (F)		Uterine canal (C)		Cervical os (O)	
	AP	CC	AP	CC	AP	CC
Grand-mean (mm)	-4.6	7.8	-4.8	5.7	2.4	1.5
Mean-range (mm)	14.5	24.4	13.1	15.7	11.2	11.3
⁹⁰ PI (mm)						
Negative	-19.4	-21.8	-24.2	-11.0	-11.4	-11.9
Positive	10.7	37.6	15.2	21.9	16.6	15.2

Table 4. Trends in interscan motion over time during radiotherapy course

Scan	Mean deviation relative to scan 1 (cm)					
	Uterine fundus (F)		Uterine canal (C)		Cervical os (O)	
	AP	CC	AP	CC	AP	CC
2	-2.3	-0.3	-3.1	0.3	0.6	0.8
3	-2.8	3.9	-2.7	3.0	3.0	1.7
4	-6.6	6.4	-4.9	4.0	2.9	0.4
5	-5.2	15.3	-5.4	10.4	3.4	3.3
6	-5.0	15.1	-6.6	10.4	3.2	2.4
P	0.17	<0.001	0.06	<0.001	0.18	0.29

Interfractional motion margin

Fundus 1-4 cm

Canal 1-2.5 cm

Os 1-1.5 cm

Intrafractional motion margin

Fundus 1 cm

Canal 0.5 cm

Os 0.5 cm

Intrafractional movements of cervix

	Mediolateral (mm)	Antero-posterior (mm)	Cranio-caudal (mm)
Lee, 2004	10	16	8
Yamamoto,2004	1.9-2.5	1.4-3.4	2.4-4.2
Raj, 2005	ND	1.4-5.1	2.9-3.9

ASSESSMENT OF ORGAN MOTION IN POSTOPERATIVE ENDOMETRIAL AND CERVICAL CANCER PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPY

ELEANOR E. R. HARRIS, M.D., KUJTIM LATHI, M.S., CHAD RUSTHOVEN, B.S., KEN JAVEDAN, PH.D., AND KENNETH FORSTER, PH.D.

Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1-6, 2011

Purpose: Intensity-modulated radiation therapy (IMRT) may be useful to reduce toxicity in gynecologic cancer patients requiring postoperative pelvic irradiation. This study was undertaken to quantify vaginal wall organ motion during the course of postoperative pelvic irradiation using pelvic IMRT.

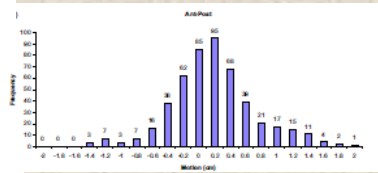
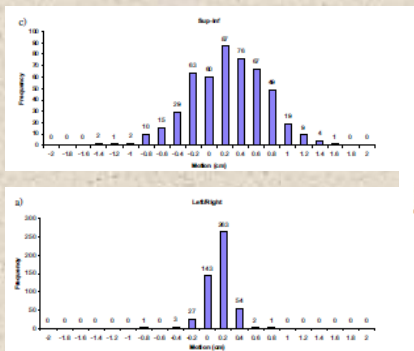


Table 1. Directional organ motion

	Mean (mm)	Median (mm)	Standard deviation (mm)	Range (mm)	95% Within (mm)
Left-right	1.2	1.1	1.0	0-8.1	3.1
Superoinferior	4.0	3.5	2.9	0-15	9.5
Anteroposterior	4.0	2.8	3.7	0-19.3	12.1
Total motion	5.8	4.6	4.7	0-25.8	15.7

Table 2. Distribution of mean deformation and excursions <10 mm for the study cohort

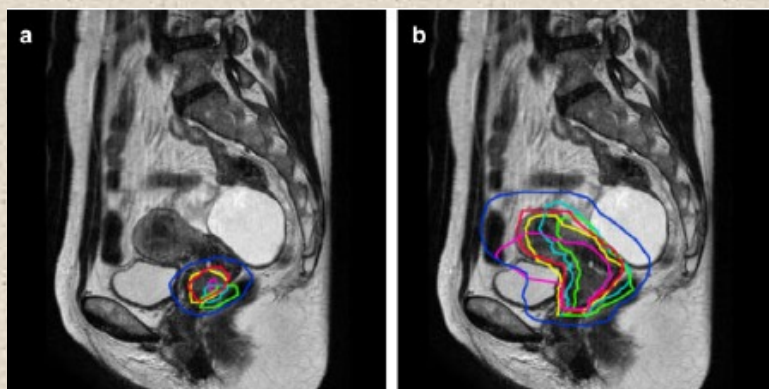
Patient	Mean deformation (mm)	SD (mm)	% MV CTs with distortions ≥ 10 mm
1	2.7	2.1	0
2	5.4	2.9	10
3	2.1	1.7	0
4	1.8	1.7	0
5	2.4	1.5	0
6	2.4	5.1	3
7	3.9	3.9	3
8	8.1	5.1	38
9	6.6	5.1	22
10	7.8	7.1	31
11	5.3	5	13
12	2	1.7	1
13	1.9	1.3	0
14	4.4	4.1	4
15	3.5	1.9	0
16	8.3	5.2	39
17	2.3	1.5	0
18	2.7	1.9	0
19	2.9	3	3
20	2.3	1.3	0
21	3.5	2.4	1
22	2.9	2.5	1
Total	3.9	3.1	8

mean deformation across all daily images for all patients was 3.9 mm (range 0-27.5 mm)

Distortions greater than 10 mm in 17% of patients

Motion and deformation of the target volumes during IMRT for cervical cancer: What margins do we need?

Linda van de Bunt^{a,*}, Ina M. Jürgenliemk-Schulz^a, Gérard A.P. de Kort^b,
Judith M. Roesink^a, Robbert J.H.A. Tersteeg^a, Uulke A. van der Heide^a



MARGINS	
GTV	CTV
Ant 12 mm	24 mm
Post 14 mm	17 mm
Dx 12 mm	12 mm
Sn 11 mm	16 mm
Sup 4 mm	11 mm
Inf 8 mm	8 mm

Fig. 2. (a) The pre-treatment GTV (red) and four GTVs at later time points (week 1: yellow, 2: light blue, 3: green, 4: magenta). The generic PTV is shown around the pretreatment GTV (dark blue); (b) analogous for the CTV.

Table 1
Margins around the pre-treatment GTV in the six main

Rectum volume	Margins around the pre-treat	
	Posterior	Anterior
<70 cc	7	16
>70 cc	16	5
p Value	<0.001	0.002

If the margins for the two groups are statistically different.

Table 2
Margins around the pre-treatment CTV in the six main directions for patients with a pre-treatment rectum volume <70 and >70 cc

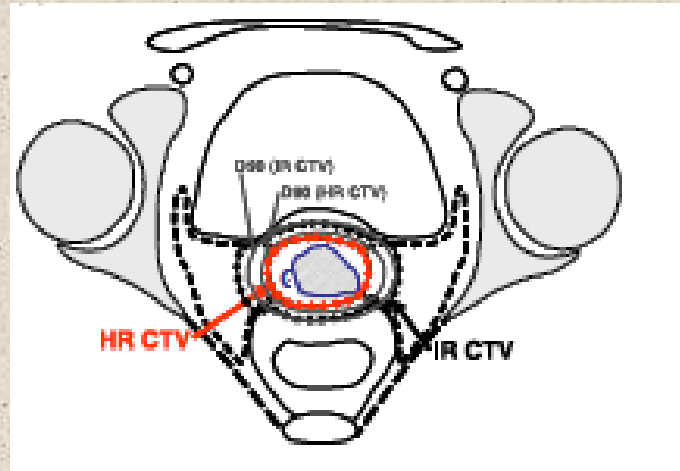
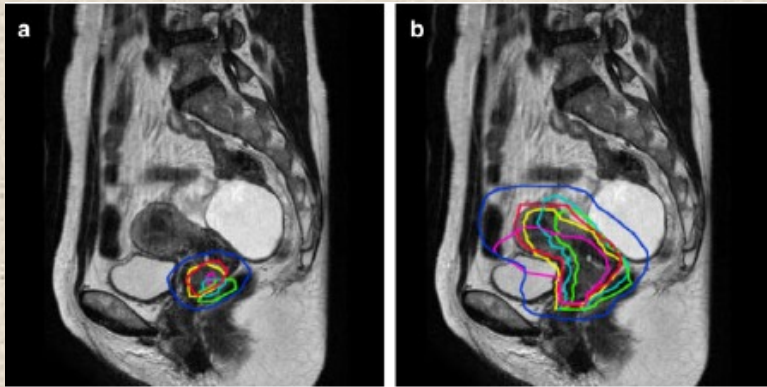
Rectum volume	Margins around the pre-treatment CTV (mm)					
	Posterior	Anterior	Left lateral	Right lateral	Superior	Inferior
<70 cc	10	24	16	12	11	6
>70 cc	20					12
p Value	<0.001	0.13	0.18	0.42	0.30	0.005

If the margins for the two groups are statistically different ($p < 0.05$) both values are reported, otherwise it is the value for the combined group.

Conclusions: We used weekly MRI scans to derive inhomogeneous PTV margins that accommodate changes in GTV and CTV. The weak correlations with rectum and bladder volume suggest that measures to control filling status of these organs may not be very effective.

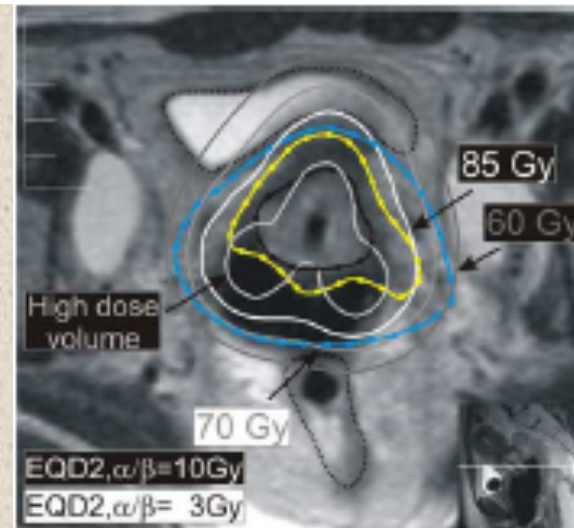
Motion and deformation of the target volumes during IMRT for cervical cancer: What margins do we need?

Linda van de Bunt^{a,*}, Ina M. Jürgenliemk-Schulz^a, Gérard A.P. de Kort^b,
Judith M. Roesink^a, Robbert J.H.A. Tersteeg^a, Uulke A. van der Heide^a



BRACHYTHERAPY

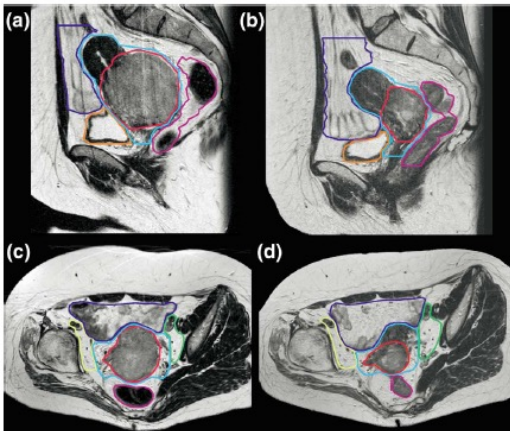
NO Internal margin
No Set-up margin



CONVENTIONAL, CONFORMAL, AND INTENSITY-MODULATED RADIATION THERAPY TREATMENT PLANNING OF EXTERNAL BEAM RADIOTHERAPY FOR CERVICAL CANCER: THE IMPACT OF TUMOR REGRESSION

LINDA VAN DE BUNT, M.D.,* UULKE A. VAN DER HEIDE, PH.D.,* MARTIJN KETELAARS, PH.D.,*
GERARD A. P. DE KORT, M.D.,† AND INA M. JÜRGENLIEMK-SCHULZ, M.D., PH.D.*

Int. J. Radiation Oncology Biol. Phys., Vol. 64, No. 1, pp. 189–196, 2006



ADAPTIVE RADIOTHERAPY

Table 3. First and second plans on intratreatment magnetic resonance images*

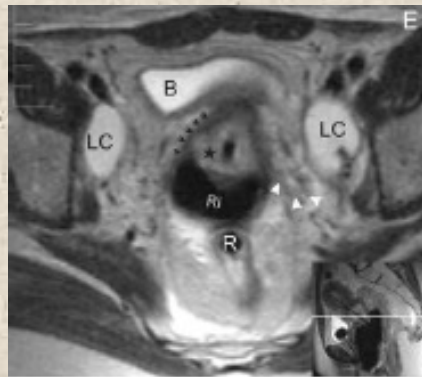
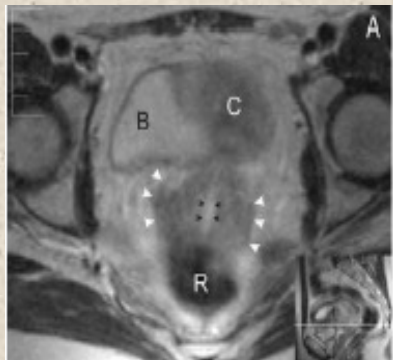
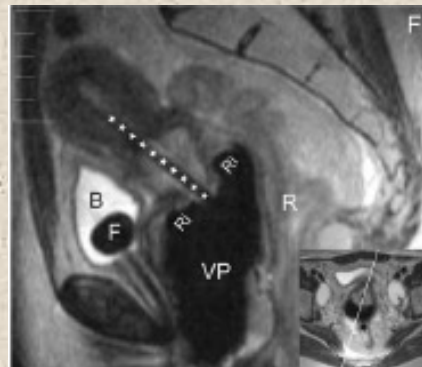
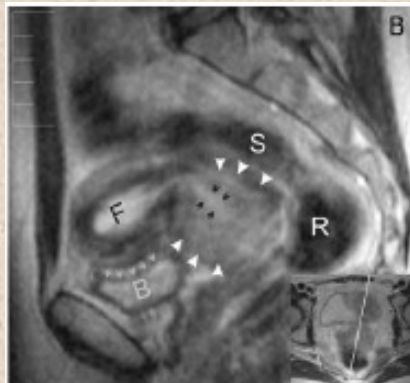
Average volume in cc	First conformal	Second conformal	<i>p</i> Value	First IMRT	Second IMRT	<i>p</i> Value
Bowel	425 (53–837)	429 (30–786)	0.8	234 (28–453)	232 (19–389)	0.6
Bladder	83 (12–209)	78 (15–206)	0.1	58 (7–115)	53 (10–121)	0.2
Rectum	83 (22–156)	79 (22–130)	0.02	75 (20–145)	67 (15–106)	0.009

Conclusions: Intensity-modulated radiation therapy is superior in sparing of critical organs compared with conventional and conformal treatment, with adequate coverage of the target volumes. Intensity-modulated radiation therapy remains superior after 30 Gy external beam radiation therapy, despite tumor regression and internal organ motion. Repeated IMRT planning can improve the sparing of the bowel and rectum in patients with substantial tumor regression. © 2006 Elsevier Inc.

Image guided adaptive brachytherapy

IGABT

diagnosi



**Target adattato al tumore
successive frazioni
Brachiterapia**

Image-guided adaptive brachytherapy

CCR	90%
LC	82%
G3-G4	2%

3-yrs

Dose escalation > 10% con tossicità < 5%

Guadagno sopravvivenza 10-20%

Potter, 2007

Image-guided adaptive brachytherapy

high-tech EBRT

CCR	90%
LC	82%
G3-G4	2%
	3-yrs

???

Image-guided adaptive brachytherapy

CCR	90%
LC	82%
G3-G4	2%
	3-yrs

high-tech EBRT

SBRT

una “ragionevole”
alternativa alla
Brachiterapia 3D

NECESSARI STUDI DI CONFRONTO

HIGH TECH BT

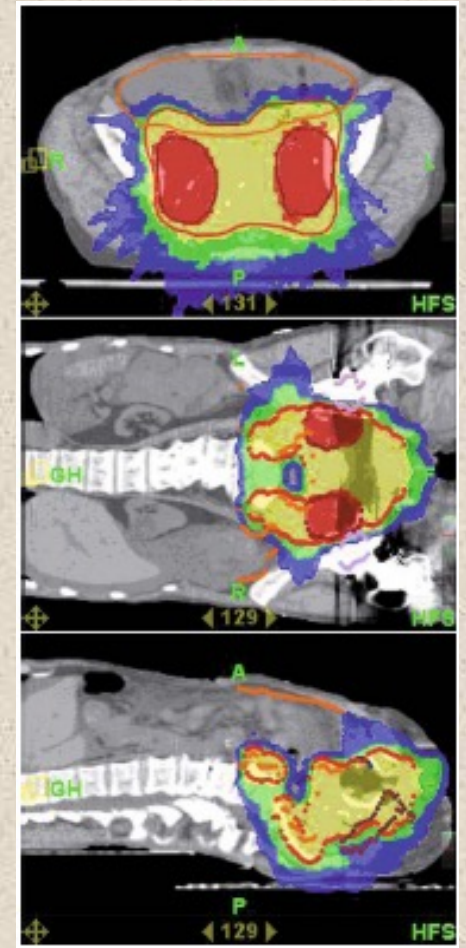
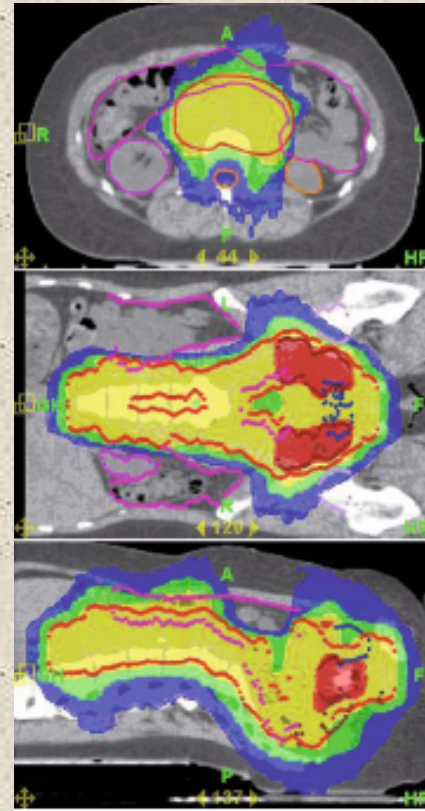
HIGH TECH EBRT

Alternativa?

Helical Tomotherapy in Cervical Cancer Patients

Simultaneous Integrated Boost Concept: Technique and Acute Toxicity

Strahlenther Onkol 2010;186:572-9



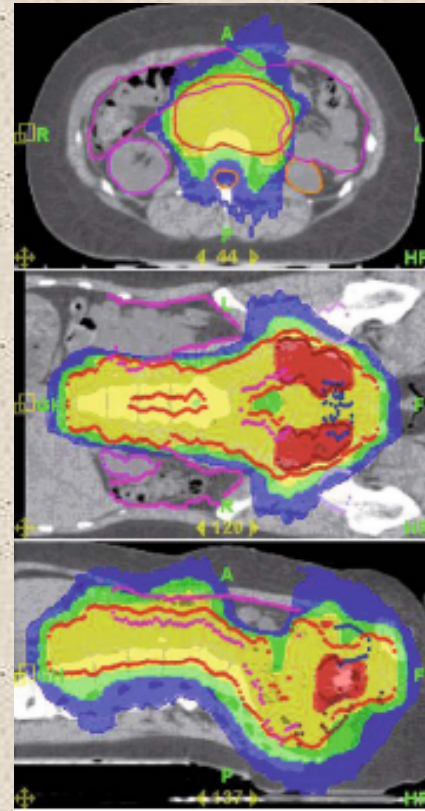
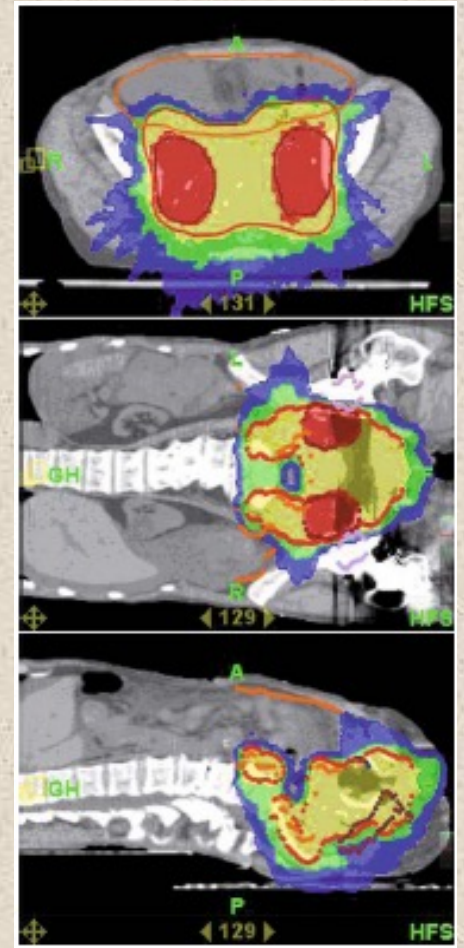
INTEGRAZIONE

high-tech EBRT con high tech BT

Helical Tomotherapy in Cervical Cancer Patients

Simultaneous Integrated Boost Concept: Technique and Acute Toxicity

Strahlenther Onkol 2010;186:572-9



con
Brachiterapia
IGABT

INTEGRAZIONE

high-tech EBRT con high tech BT

SPLIT-FIELD HI
FOI

HELICAL TOMOTHERAPY WITH SIMULTANEOUS INTEGRATED BOOST AFTER
LAPAROSCOPIC STAGING IN PATIENTS WITH CERVICAL CANCER: ANALYSIS OF
FEASIBILITY AND EARLY TOXICITY

ALBERT J. CHANG, M

PROSPECTIVE
CHEMOT

**Whole pelvic helical tomotherapy for locally advanced cervical
cancer: technical implementation of IMRT with helical
tomotherapy**

WALDEMAR

JULIE K. SCHWAI

Chen-Hsi Hsieh^{1,3}, Ming-Chow Wei², Hsing-Yi Lee¹, Sheng-Mou Hsiao²,
Chien-An Chen¹, Li-Ying Wang⁷, Yen-Ping Hsieh⁸, Tung-Hu Tsai^{3,9},
Yu-Jen Chen^{*3,4,5,6} and Pei-Wei Shueng^{*1,10,11}

autore	N° pts	CHT	Dose Gy	target	BT	toxicity
Marnitz, Strahl Oncol2010	20	CDDP	50.9 59.6	GTV CTV=GTV+5 mm PTV=CTV+10mm	HDR RMbased 5 Gy x 5	GI G3=0
Schwartz Int J Rad Oncol Biol Phys 2010	24	CDDP No CHT	51.2	PTV nodal PTV vaginal with Vaginal dilatator	HDR 3Gyx6	GI G3=14%
Chang Int J Rad Oncol Biol Phys 2011	15	CDDP	50 70	CTV PTV=CTV+7mm	HDR RM based 6.5 Gy x 6	GI G3=7%
Chen-Hsi Hsieh Rad onco 2009	10	CDDP	50.4	CTV PTV=CTV+7mm	HDR 6Gyx5	GI G3=0



Associazione
Italiana
Radioterapia
Oncologica

Genova, 19-22 Novembre 2011
Porto Antico di Genova
Centro Congressi

grazie per l'attenzione

Vitaliana De Sanctis
Cattedra di Radioterapia
Facoltà di Medicina e Psicologia
Università "Sapienza"
Roma