Cancer du col utérin.

Relation dose/contrôle local.

Sophie ESPENEL

Janvier 2021

Pourquoi ?

Quel niveau de preuve ?

Etudes rétrospectives

- Amélioration continue du contrôle local ⇔ escalade de dose
- Diminution continue des toxicités sévères
- Amélioration définition des volumes tumoraux
- Amélioration de la conformation des implants.

Etudes prospectives EMBRACE I et II

- Validation de critères dosimétriques.

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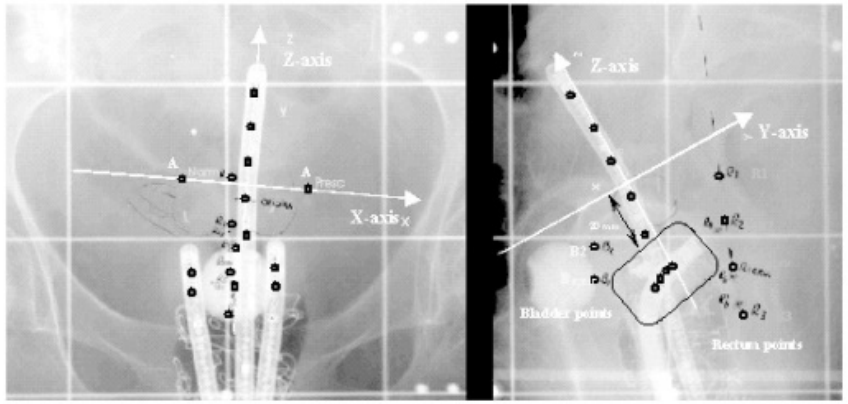
Impact of dose in outcome of irradiation alone in carcinoma of the uterine cervix: analysis of two different methods

Carlos A. Perez • Seymour Fox • Mary Ann Lockett • ... Andrew Galakatos • Ming-Shian Kao • Jeffrey Williamson • Show all authors

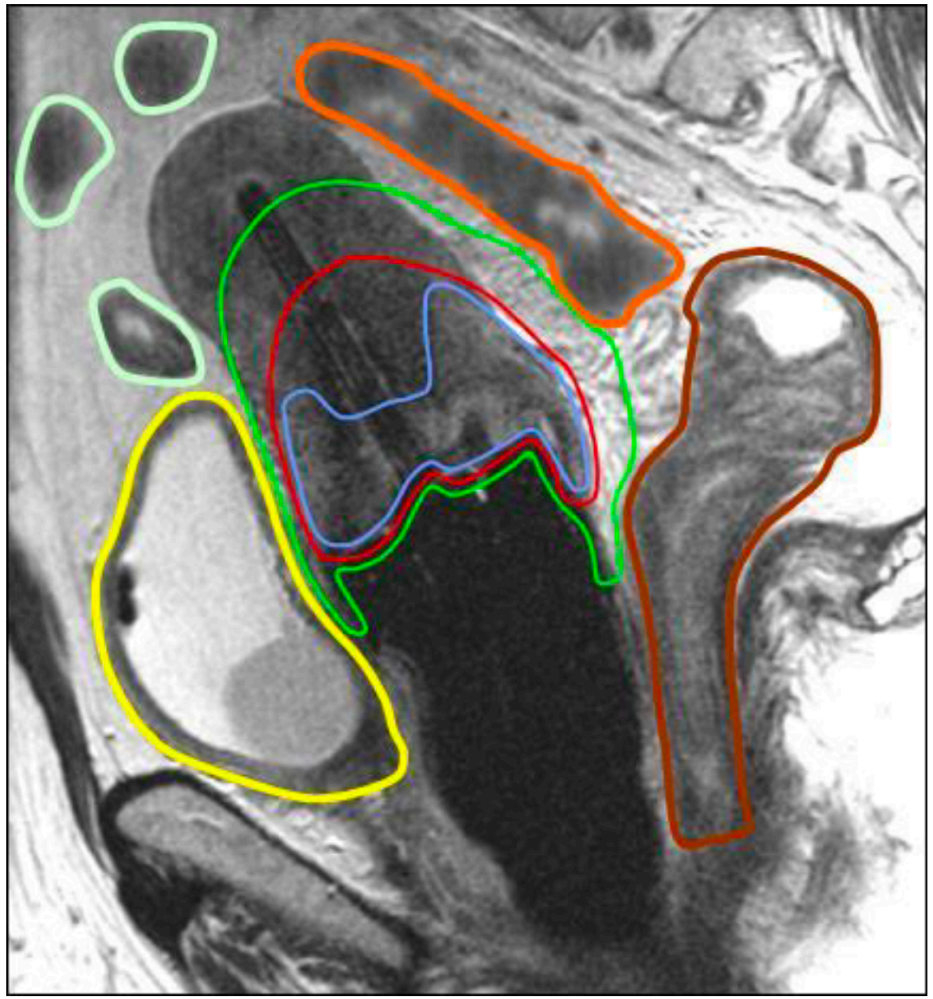
1211 patientes cancer du col

Rechutes loco régionales ⇔ dose



Dose point A	Stade IIB		Stade III	
	n = 347	Rechutes (%)	n = 282	Rechutes (%)
< 60 Gy	8/12	67 % *p < 0.01*	18/25	72 % *p < 0.01*
60 – 90 Gy	61/261	23 %	71/180	39 %
> 90 Gy	10/74	14 %	27/ 77	35 %

Perez *et al*. IJROBP 1991



Bleu : GTV
Rouge : CTV HR
Vert : CTV IR

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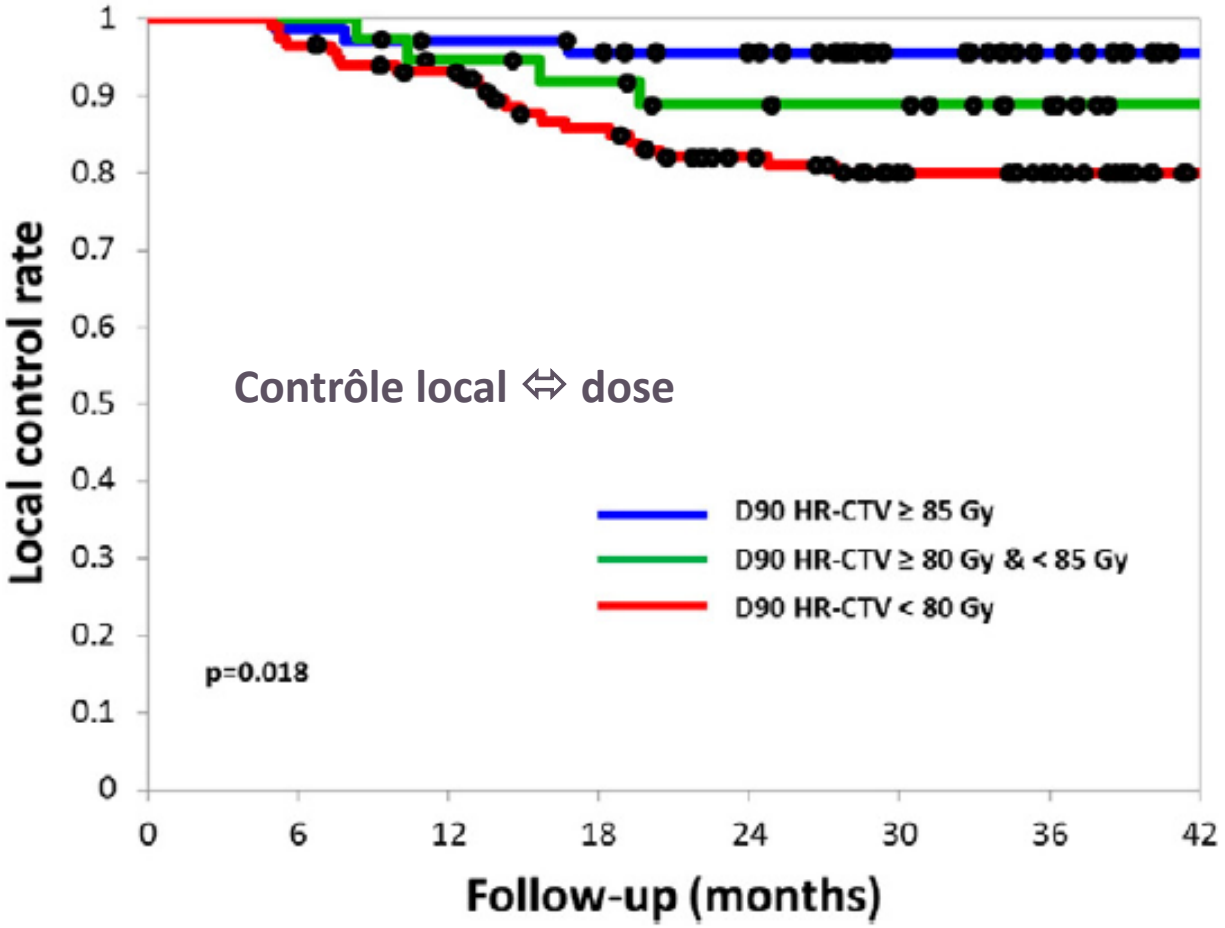
Clinical outcomes of definitive chemoradiation followed by intracavitary pulsed-dose rate image-guided adaptive brachytherapy in locally advanced cervical cancer

Pauline Castelnau-Marchand [a], Cyrus Chargari [a,b], Pierre Maroun [a], Isabelle Dumas [c], Eleonor Rivin del Campo [a], Kim Cao [a], Claire Petit [a], Florent Martinetti [c], Alain Tafo-Guemnie [c], Dimitri Lefkopoulos [b,c], Philippe Morice [d], Christine Haie-Meder [a], Renaud Mazeron [a,b,*]



Castelnau-Marchand *et al.* Gynecol Oncol 2015

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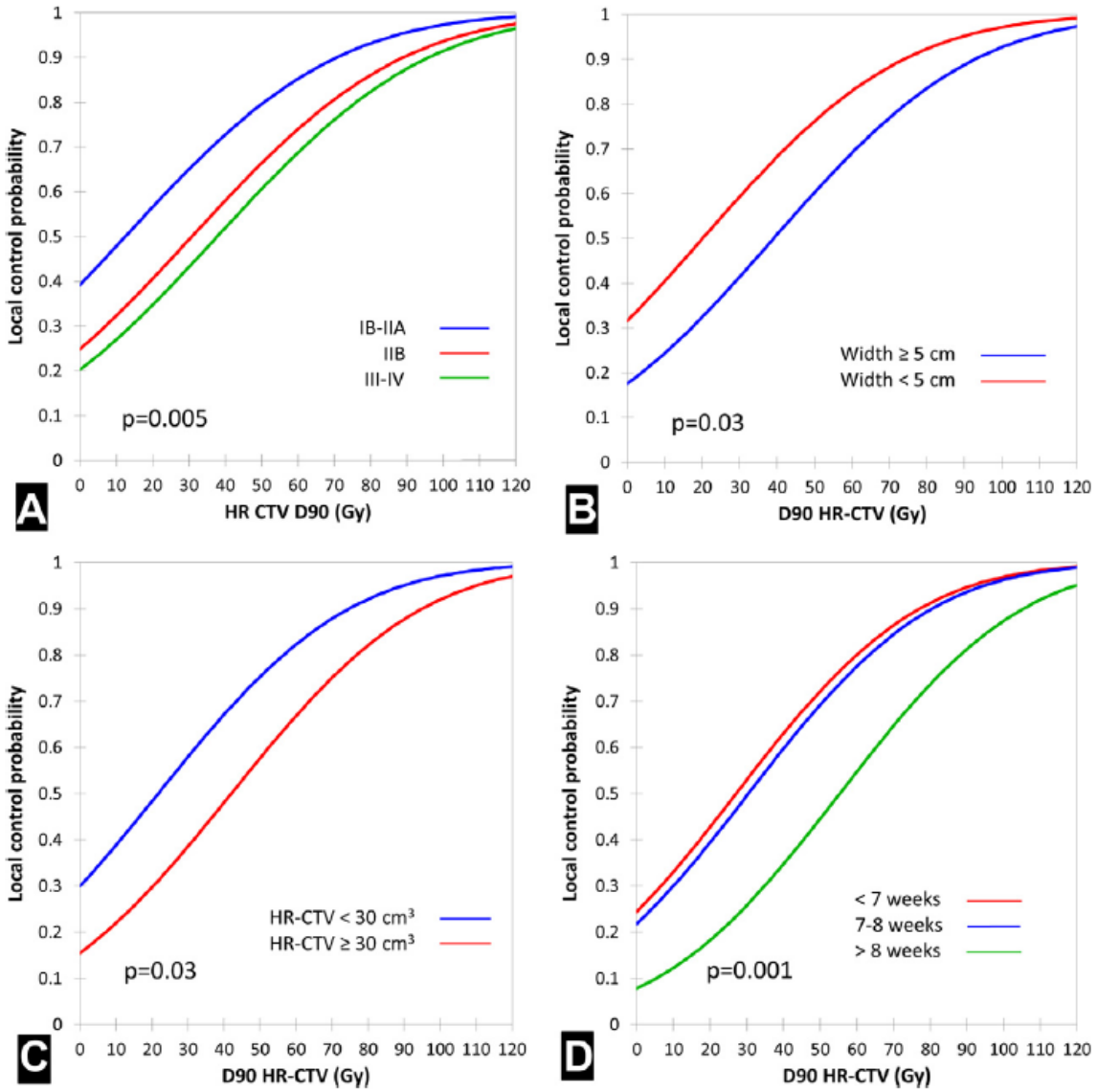
GRAND PARIS

Impact of treatment time and dose escalation on local control in locally advanced cervical cancer treated by chemoradiation and image-guided pulsed-dose rate adaptive brachytherapy



Mazeron *et al.* Radiother Oncol 2015

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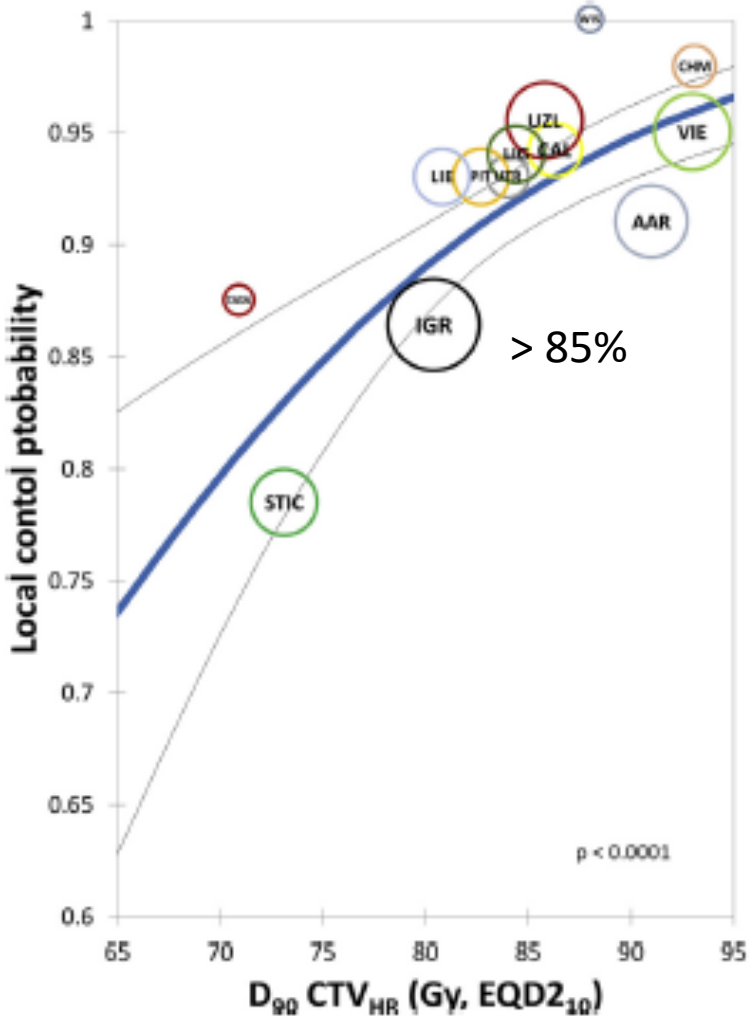
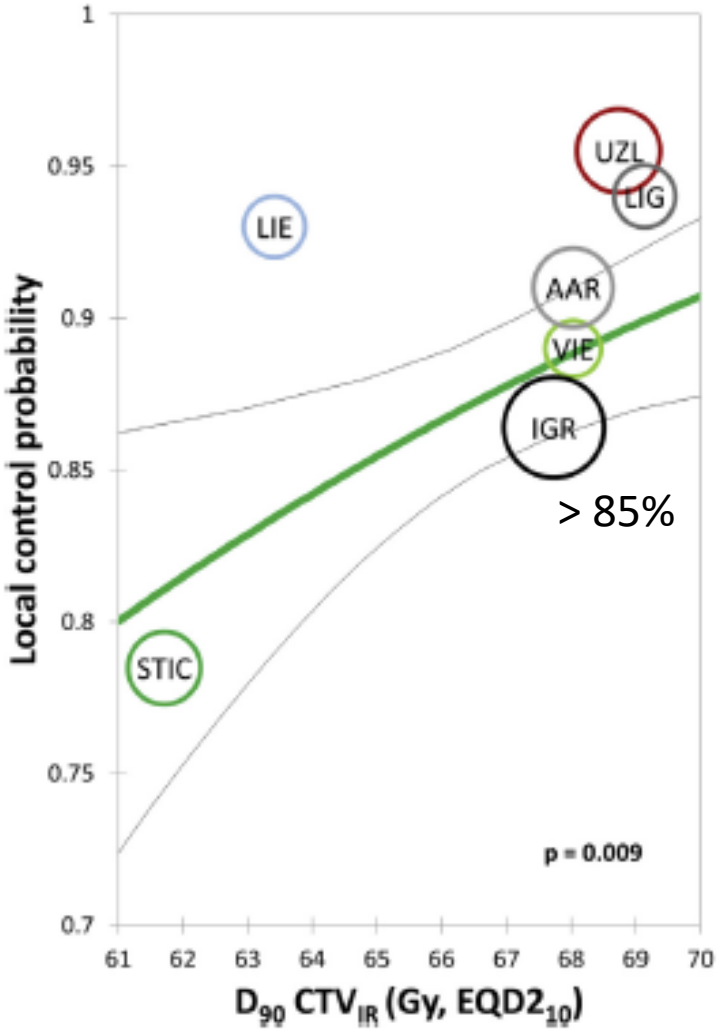
GRAND PARIS

Tumor dose–volume response in image-guided adaptive brachytherapy for cervical cancer: A meta-regression analysis

Renaud Mazeron[1,2,*], Pauline Castelnau-Marchand[1], Alexandre Escande[1], Eleonor Rivin del Campo[1], Pierre Maroun[1], Dimitri Lefkopoulos[2,3], Cyrus Chargari[1,2,4], Christine Haie-Meder[1]





Mazeron *et al.* Radiother Oncol 2015

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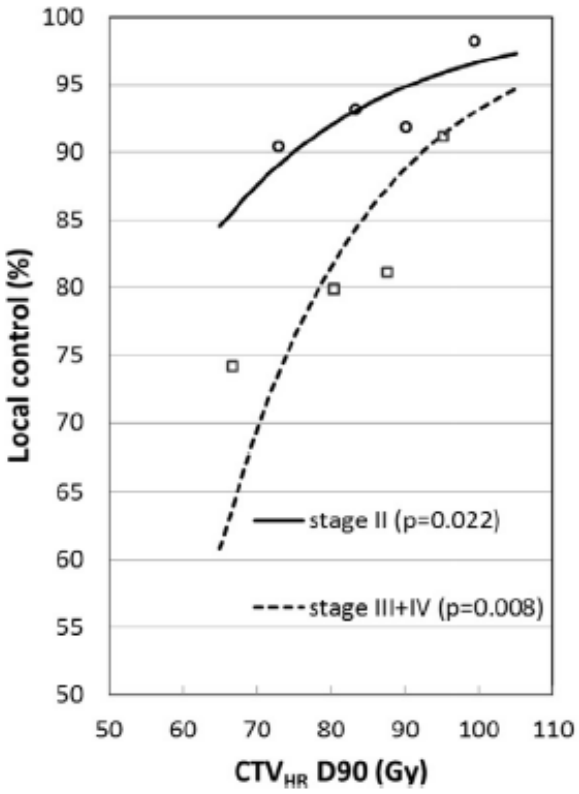
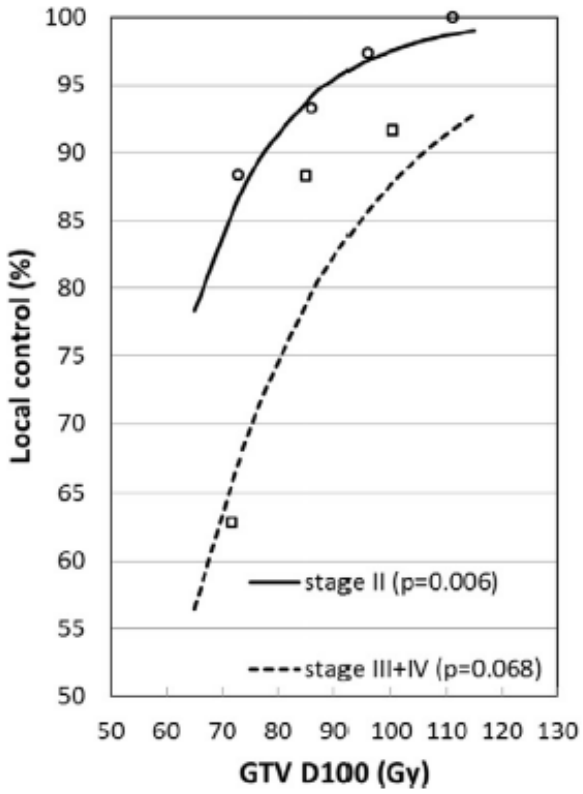
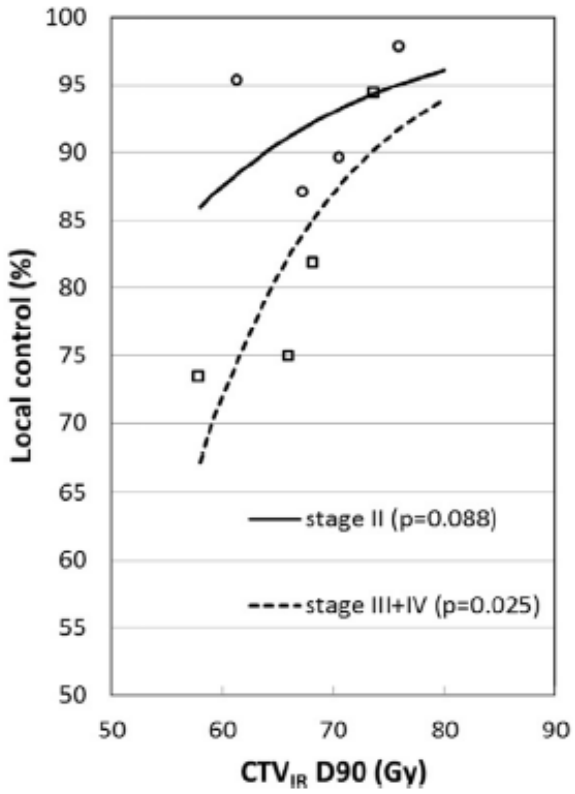
RETRO EMBRACE
An intErnational study on MRI-guided BRachytherapy in locally Advanced CErvical cancer

About Retro-Embrace | Contacts | Login

Corrélation dose ⇔ contrôle local







Tanderup *et al.* Radiother Oncol 2016

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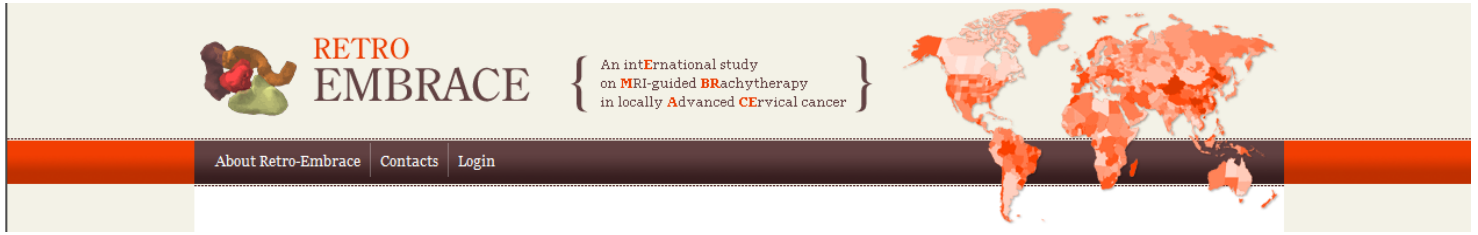
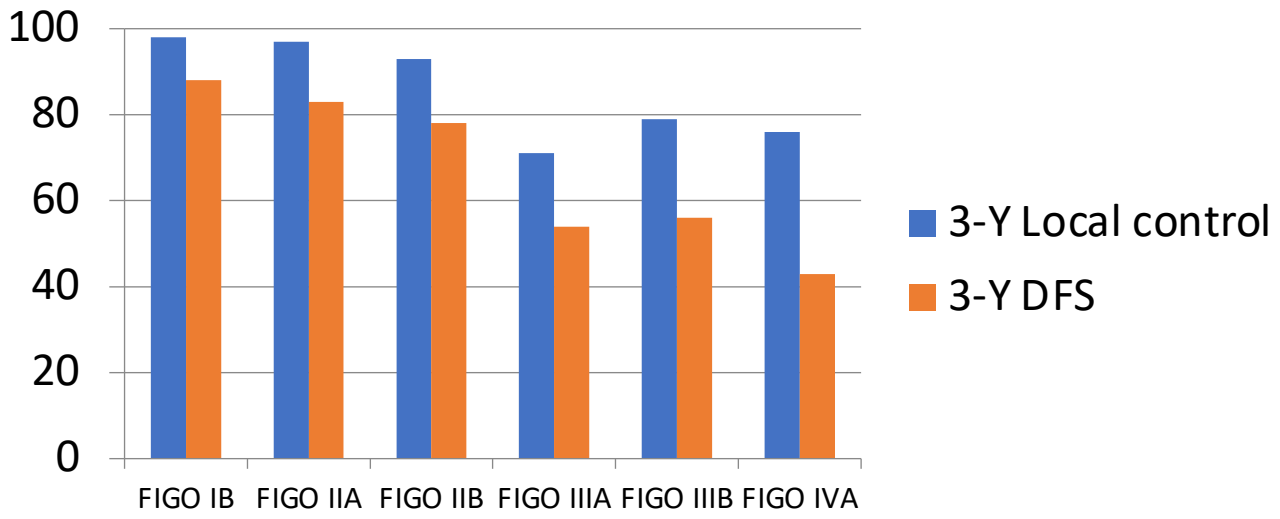


FIGO stage	Number of patients	Total number of local failures	Total number of pelvic failures	Number of patients with any failure	Number of patients with no evidence of disease	Mean D90 HRCTV in Gy (±SD)	Actuarial local control at 3/5 years	Actuarial pelvic control at 3/5 years	Actuarial overall survival at 3/5 years	Actuarial cancer specific survival at 3/5 years
1A	2	0	0	0	2	–	100%	100%	100%	100%
1B	123	2	4	19	104	93 ± 17	98%/98%	96%/96%	88%/83%	93%/90%
2A	42	3	4	9	33	89 ± 16	97%/94%	95%/92%	83%/80%	87%/84%
2B	368	28	42	97	271	88 ± 14	93%/91%	89%/87%	78%/70%	83%/77%
3A	23	5	6	13	10	83 ± 12	71%/71%	66%/66%	54%/42%	54%/48%
3B	145	28	36	68	77	83 ± 13	79%/75%	73%/67%	56%/42%	65%/53%
4A	23	3	3	13	10	78 ± 13	76%/76%	76%/76%	43%/32%	53%/ 40%
4B	5	0	1	3	2	78 ± 2	–	–	–	
Total	731	69	96	222	509	87 ± 15	91%/89%	87%/84%	74%/65%	79%/73%



Tanderup *et al.* Radiother Oncol 2016

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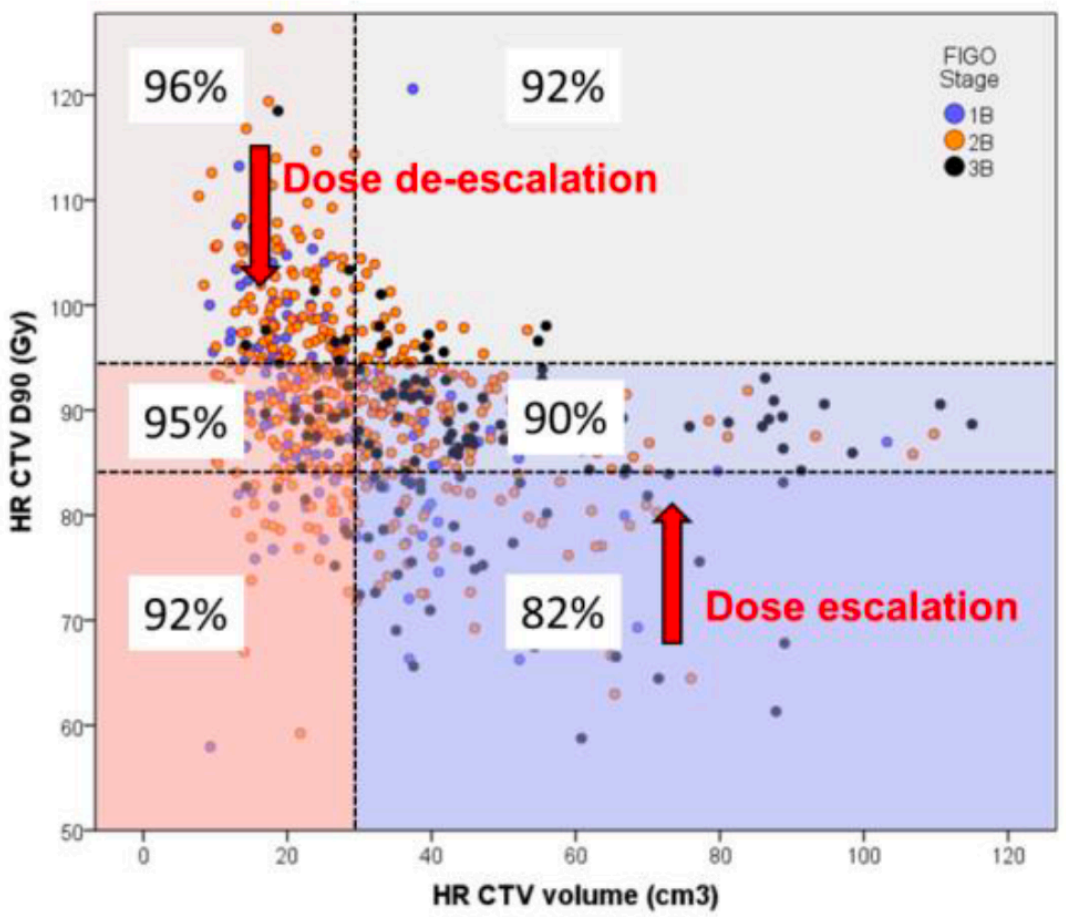
N = 1416



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Embrace II

	HR-CTV **D90** (Gy)	HR-CTV **D98** (Gy)	GTV **D98** (Gy)	IR-CTV **D98** (Gy)	Vessie **D2cm³** (Gy)	Rectum **D2cm³** (Gy)	Grêle-Sigm **D2cm³** (Gy)	ICRU rectum (Gy)
Optimal	**90-95**	> 75	> 95	> 60	**< 80**	**< 65**	**< 70**	< 65
Acceptable	> 85	--	> 90	--	< 90	**<** 75	< 75	< 75

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Pour qui ?

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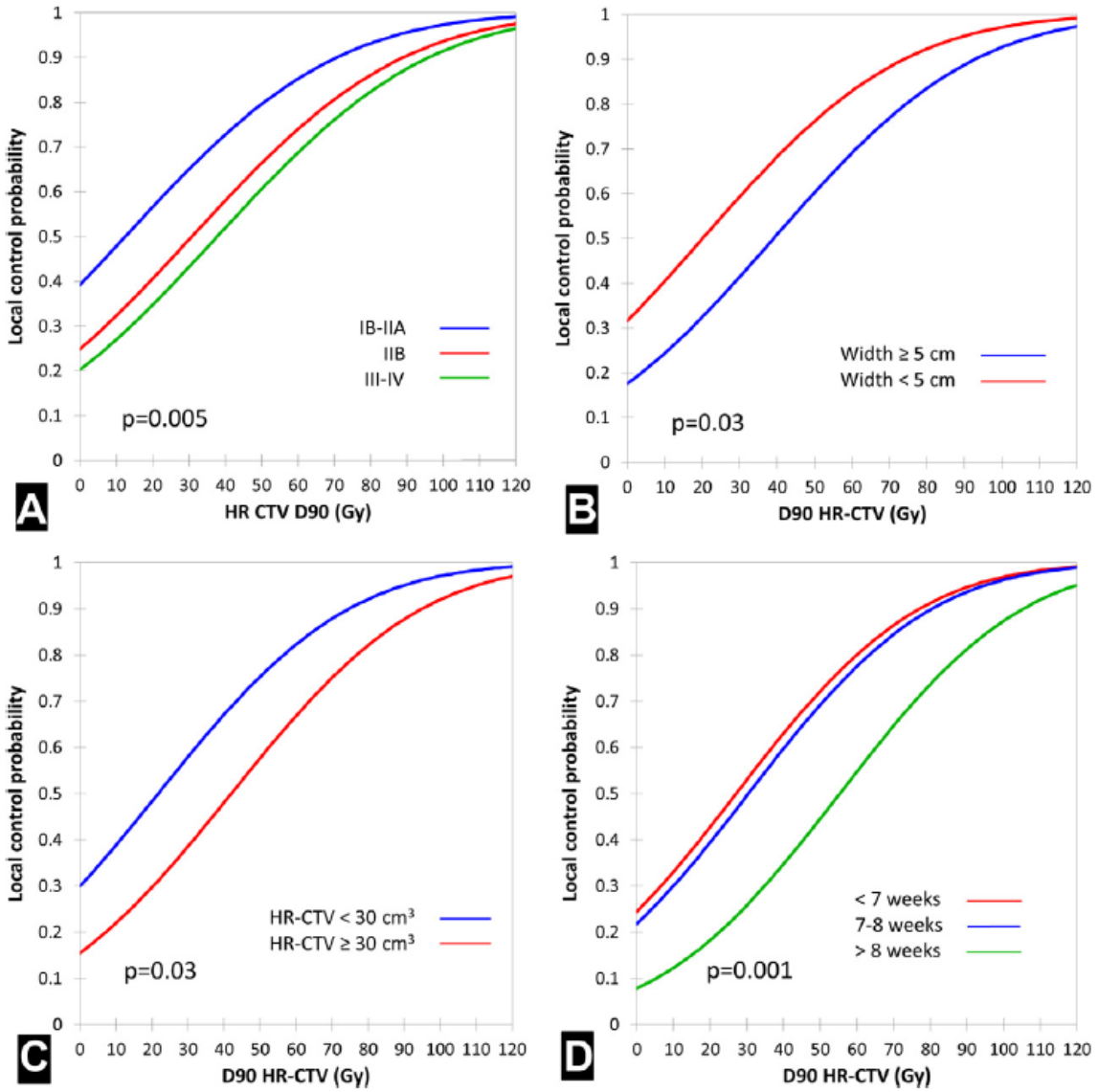
Impact of treatment time and dose escalation on local control in locally advanced cervical cancer treated by chemoradiation and image-guided pulsed-dose rate adaptive brachytherapy



Mazeron *et al.* Radiother Oncol 2015

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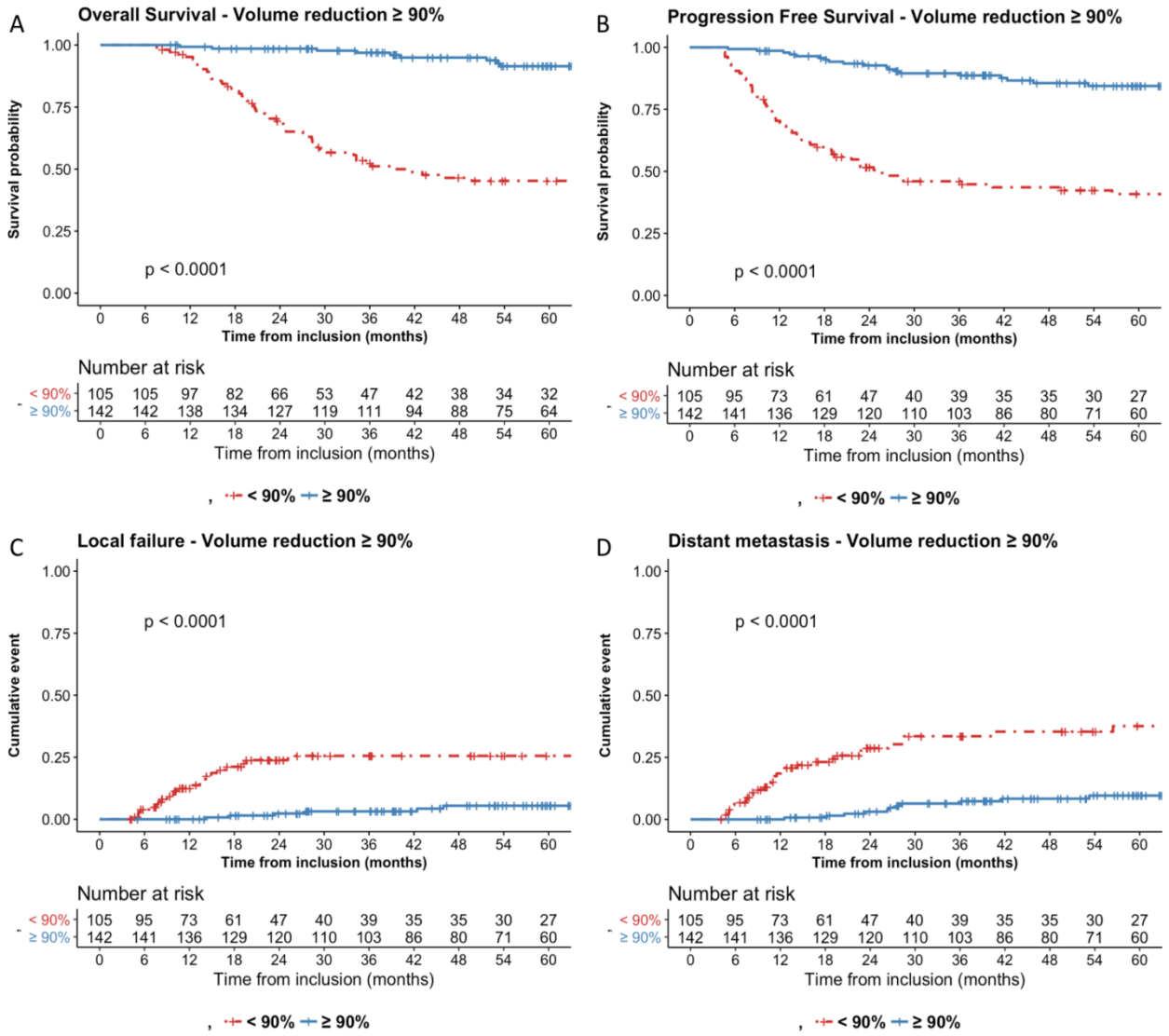
Tumor Shrinkage During Chemoradiation in Locally Advanced Cervical Cancer Patients: Prognostic Significance, and Impact for Image-Guided Adaptive Brachytherapy



Schernberg *et al*. IJROBP 2018

GUSTAVE ROUSSY
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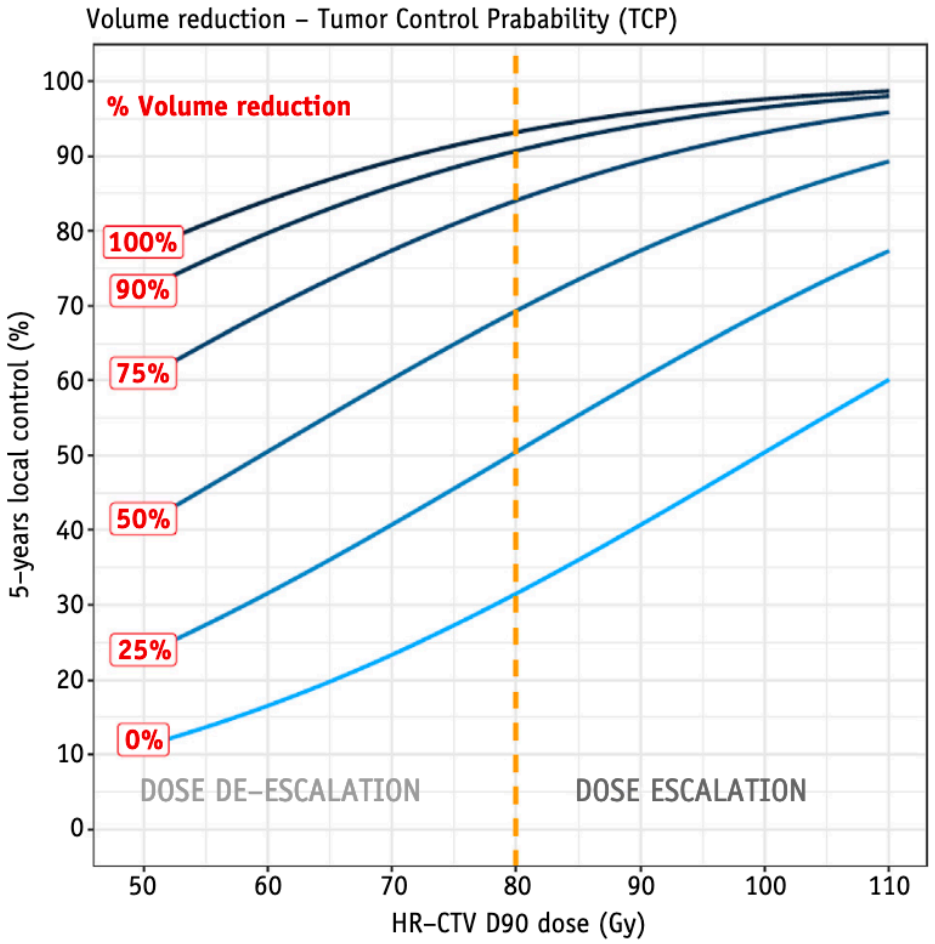
Tumor Shrinkage During Chemoradiation in Locally Advanced Cervical Cancer Patients: Prognostic Significance, and Impact for Image-Guided Adaptive Brachytherapy



Schernberg *et al*. IJROBP 2018

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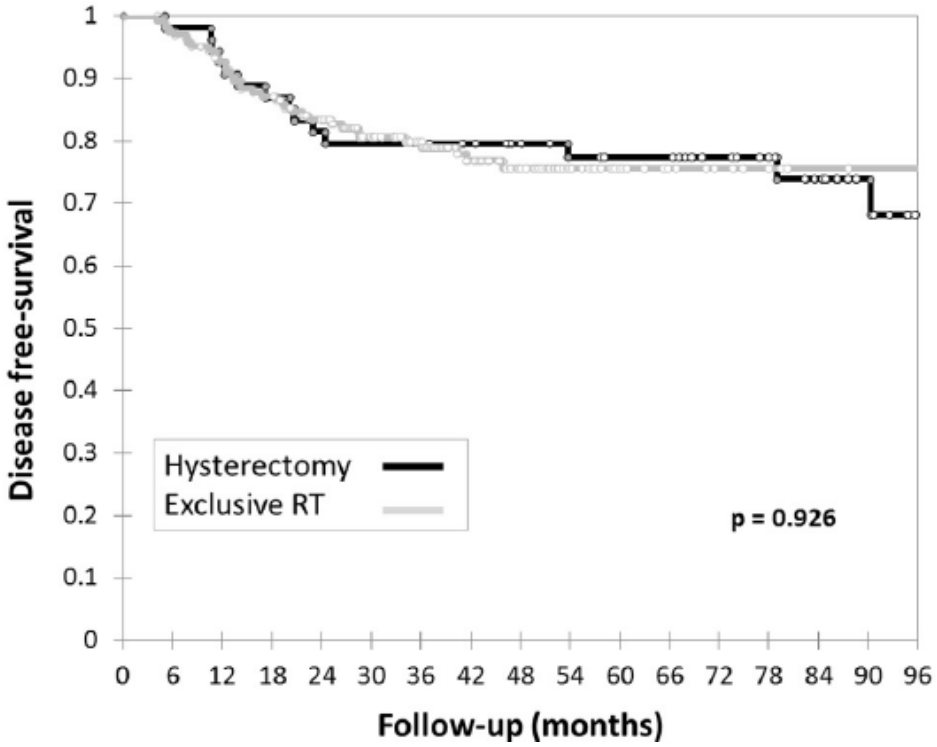
Post radiation hysterectomy in locally advanced cervical cancer: Outcomes and dosimetric impact

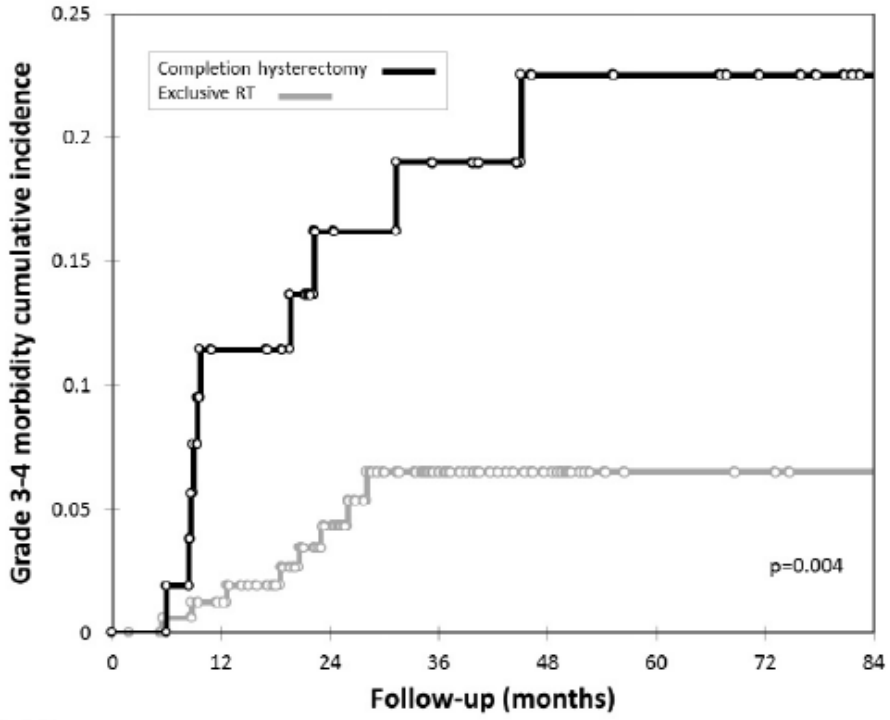
Renaud Mazeron [a,*], Sébastien Gouy [b], Cyrus Chargari [a], Eleonor Rivin del Campo [a], Isabelle Dumas [c], Augustin Mervoyer [d], Catherine Genestie [e], Enrica Bentivegna [b], Corinne Balleyguier [f], Patricia Pautier [g], Philippe Morice [b], Christine Haie-Meder [a]

Une chirurgie devenue inutile

54 patientes : chirurgie de clotûre (≠ rattrapage)

157 patientes: RT-curiethérapie exclusive





➔ **La chirurgie de clôture est devenue inutile (délétère?)**

Mazeron *et al.* Radiother Oncol 2016

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Post radiation hysterectomy in locally advanced cervical cancer: Outcomes and dosimetric impact

Renaud Mazeron [a,*], Sébastien Gouy [b], Cyrus Chargari [a], Eleonor Rivin del Campo [a], Isabelle Dumas [c], Augustin Mervoyer [d], Catherine Genestie [e], Enrica Bentivegna [b], Corinne Balleyguier [f], Patricia Pautier [g], Philippe Morice [b], Christine Haie-Meder [a]

Chirurgie de cloture

D2cm^3 = **67,8 Gy**
➔ 10 % de tox sévère

RTE / curieT exclusive

D2cm^3 = **91,9 Gy**
➔ 10 % de tox sévère

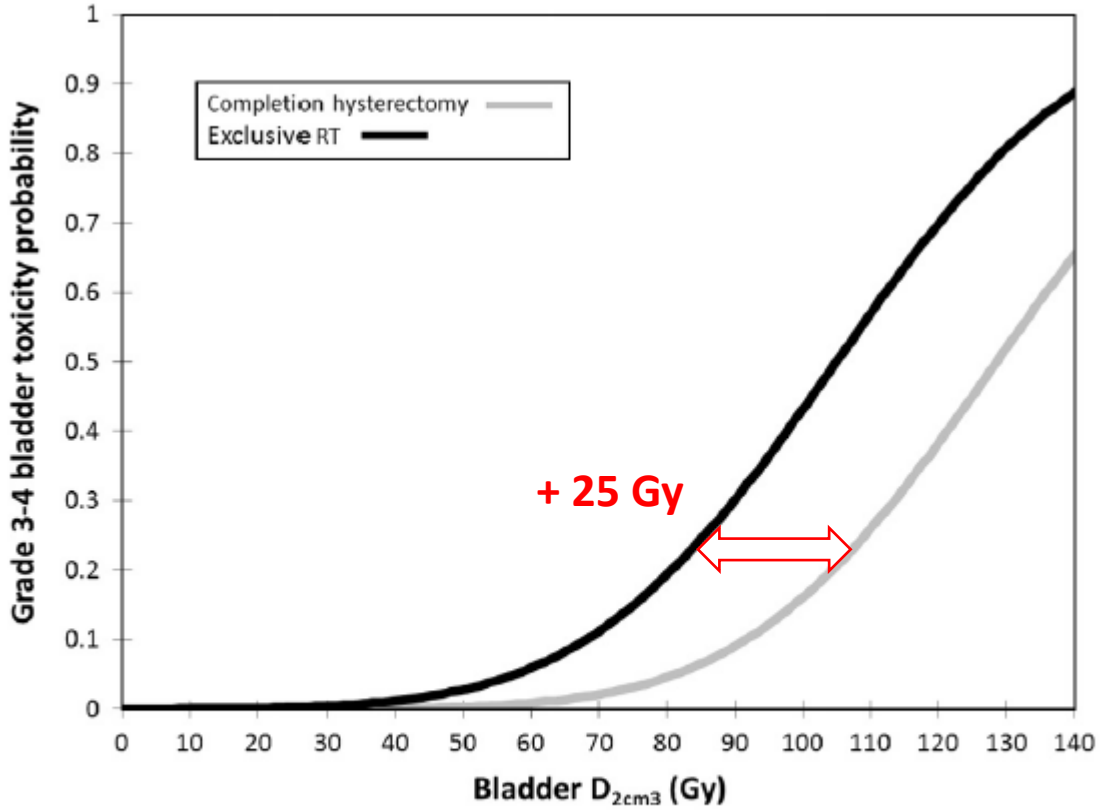

Fig. 4. Dose–volume effect relationships of the bladder. D_{2cm3}: minimal dose planned in the maximally exposed 2 cm^3 of the bladder. RT: radiotherapy.

Mazeron *et al.* Radiother Oncol 2016

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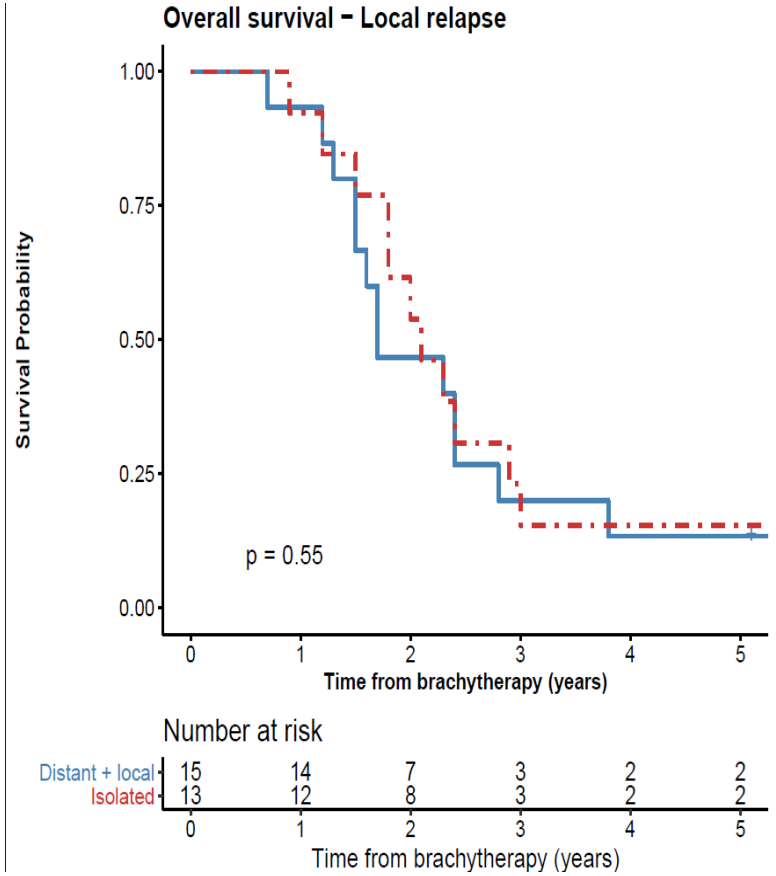
Comprehensive analysis of patient outcome after local recurrence of locally advanced cervical cancer treated with concomitant chemoradiation and image-guided adaptive brachytherapy

F. Mignot [a,*], S. Gouy [b], A. Schernberg [a], S. Bockel [a], S. Espenel [a], A. Maulard [b], A. Leary [c], C. Genestie [d], P. Annede [a], M. Kissel [a], I. Fumagalli [a], P. Pautier [c], E. Deutsch [a], C. Haie-Meder [a], P. Morice [b], C. Chargari [a,e,f]

Rechutes locales non rattrapées



Mignot *et al.* Gynecol Oncol 2020

Comment ?

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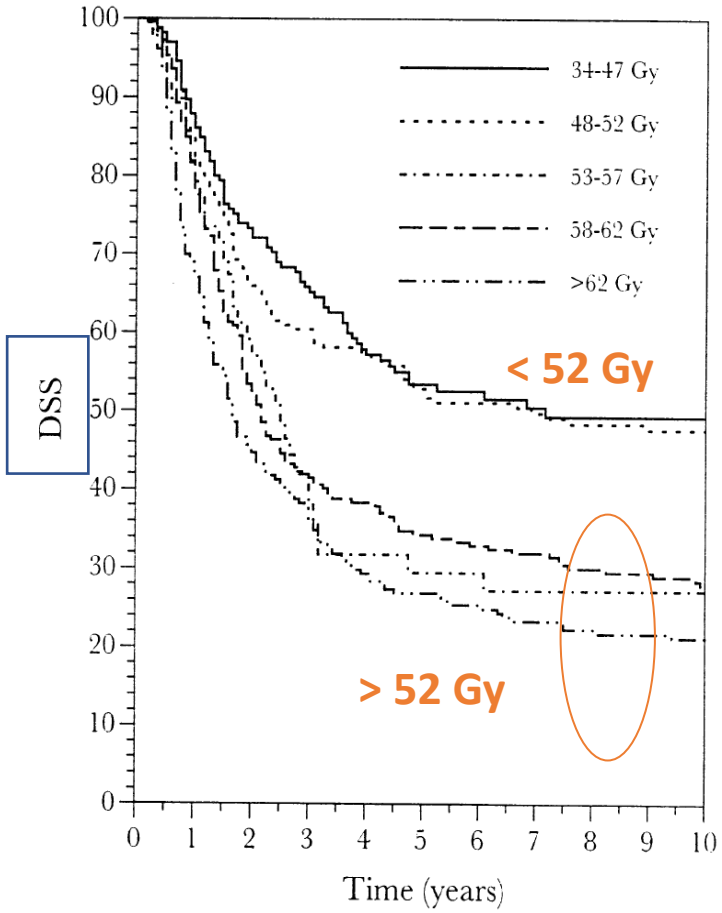
FIGO IIIB SQUAMOUS CELL CARCINOMA OF THE CERVIX: AN ANALYSIS OF PROGNOSTIC FACTORS EMPHASIZING THE BALANCE BETWEEN EXTERNAL BEAM AND INTRACAVITARY RADIATION THERAPY

MARK D. LOGSDON, M.D., AND PATRICIA J. EIFEL, M.D.

Division of Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX

- 907 patientes
- Stades IIIB
- Différentes périodes
- Doses élevées RTE
  - Morbidité (+)
  - Survie spécifique (-)



Logsdon *et al.* IJROBP, 1999

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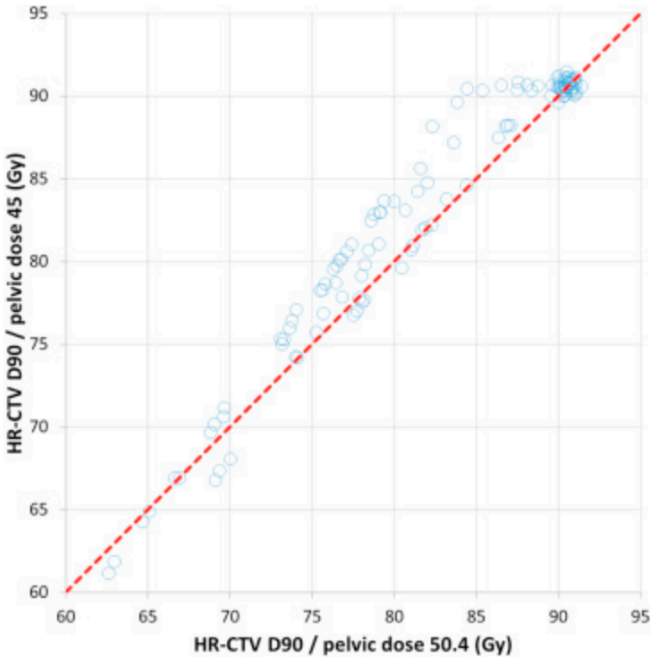
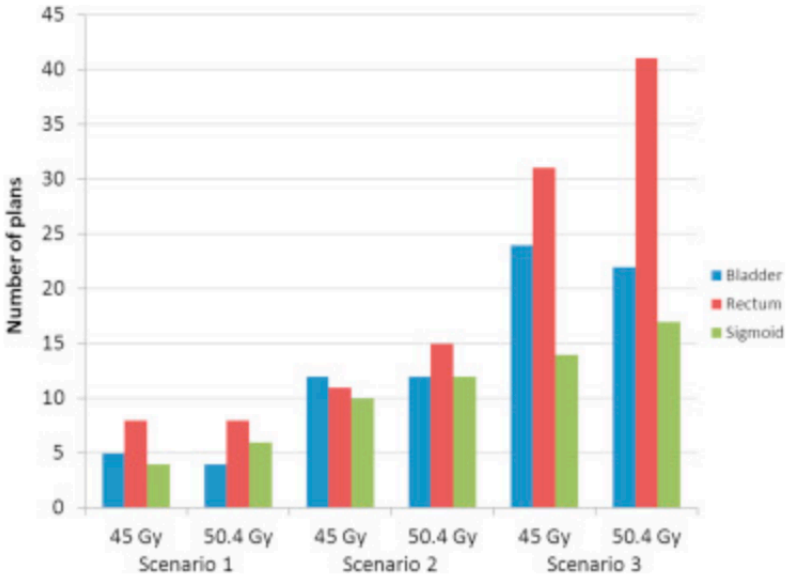
45 or 50 Gy, Which is the Optimal Radiotherapy Pelvic Dose in Locally Advanced Cervical Cancer in the Perspective of Reaching Magnetic Resonance Image-guided Adaptive Brachytherapy Planning Aims?

R. Mazeron *†, C. Petit *, E. Rivin *, E. Limkin *, I. Dumas ‡, P. Maroun *, P. Annede *, F. Martinetti ‡, T. Seisen *, D. Lefkopoulos †‡, C. Chargari *, C. Haie-Meder *





120 plans optimisés.
En faveur 45 Gy.
$D_{90}CTV_{HR}$ supérieure
Doses OAR moindres

	D90 CTV HR	D90 CTV IR	D2cc vessie	D2cc rectum	D2cc sigmoïde
S 1	85	60	90	75	75
S 2	90	60	90	75	75
S 3	90	60	80	65	70

Mazeron *et al.* Clinical Oncol 2016

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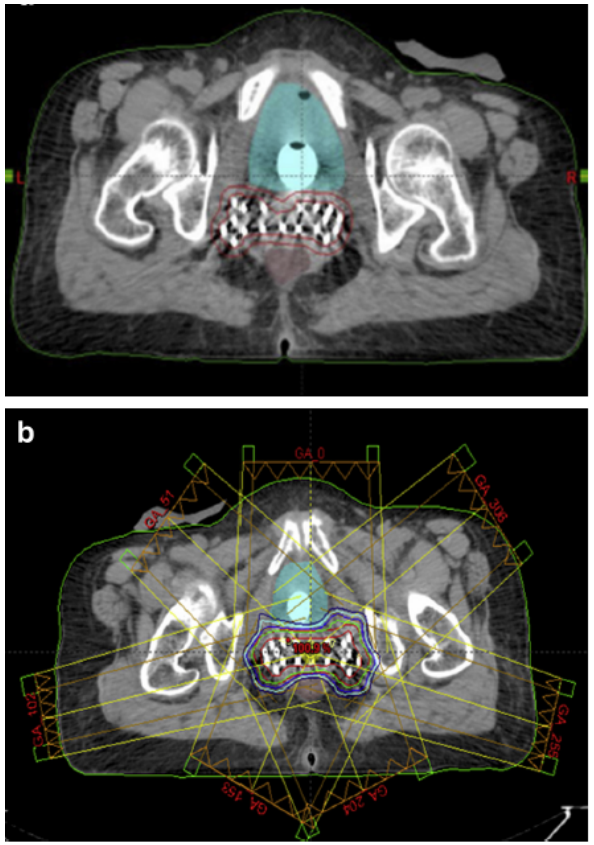
ISBT vs IMRT

HDR BT: 20 Gy en 2 fr (BED = 40 Gy)
IMRT: 33 Gy en 13 fr (BED = 41 Gy)



Interstitial brachytherapy vs. intensity-modulated radiation therapy for patients with cervical carcinoma not suitable for intracavitary radiation therapy

Table 2
Mean doses in Gray received by the PTV (BED_{10}) and the OAR (BED_3)

Parameters	IBT	IMRT	*p*-Value
PTV			
D_{95}	57.16 (±5.54)	41.47 (±1.79)	**0.003**
Minimum dose	17.63 (±1.984)	27.99 (±1.572)	**0.001**
Maximum dose	126.34 (±25.52)	50.79 (±7.81)	**0.001**
Conformity index	0.94 (±0.01)	0.908 (±0.02)	**0.034**
Bladder			
D_{max}	50.64 (±7.2)	66.31 (±2.79)	**0.004**
$D_{5\ cc}$	37.28 (±5.92)	50.04 (±7.16)	**0.05**
D_{50}	12.08 (±2.24)	27.16 (±2.61)	**0.001**
D_{75}	7.24 (±1.40)	20.83 (±4.52)	**0.001**
Rectum			
D_{max}	54.64 (±3.57)	62.63 (±3.94)	**0.02**
$D_{5\ cc}$	42.08 (±3.18)	39.32 (±2.05)	0.271
D_{50}	15.04 (±0.70)	20.79 (±5.22)	0.103
D_{75}	12.64 (±3.05)	10.84 (±0.80)	0.326
Urethra			
D_{max}	40.77 (±1.96)	34.90 (±13.01)	**0.05**
$D_{5\ cc}$	21.04 (±8.24)	24.08 (±8.06)	0.55
D_{50}	23.18 (±6.16)	30.70 (±2.78)	0.097
D_{75}	17.82 (±4.25)	26.44 (±3.22)	**0.04**

+15 Gy

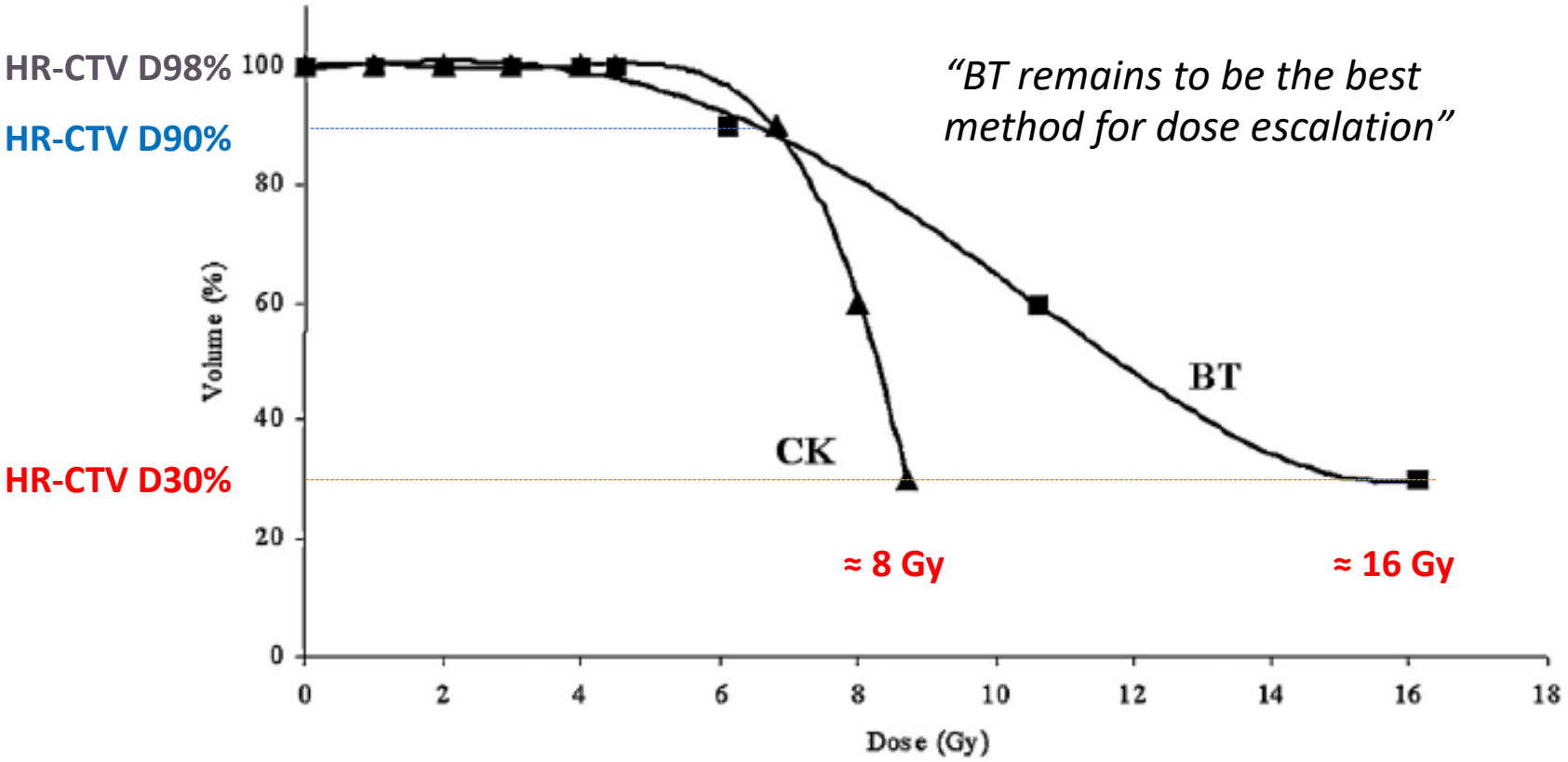
-15 Gy

-8Gy

Sharma *et al.* Brachytherapy 2013

Dosimetric comparison of MRI-based HDR brachytherapy and stereotactic radiotherapy in patients with advanced cervical cancer: A virtual brachytherapy study

Cyberknife *versus* HDR-BT: 6 x 5 Gy à la D90 du CTV HR



"BT remains to be the best method for dose escalation"

Otahal *et al.* Rep Pract Oncol Radiother

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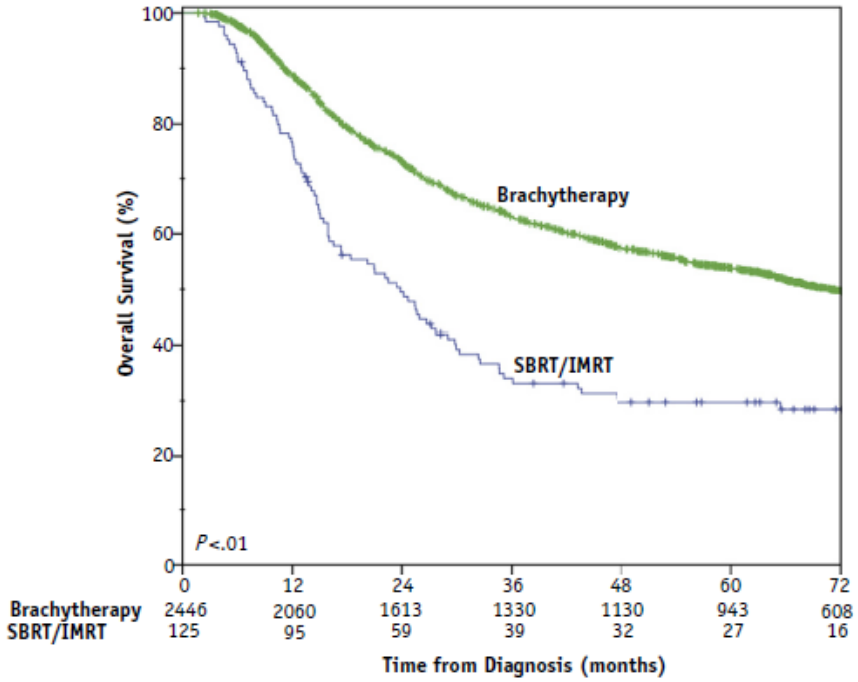
National Cancer Data Base Analysis of Radiation Therapy Consolidation Modality for Cervical Cancer: The Impact of New Technological Advancements

Beant S. Gill, MD,* Jeff F. Lin, MD,† Thomas C. Krivak, MD,‡ Paniti Sukumvanich, MD,† Robin A. Laskey, MD,† Malcolm S. Ross, MD,† Jamie L. Lesnock, MD,† and Sushil Beriwal, MD*



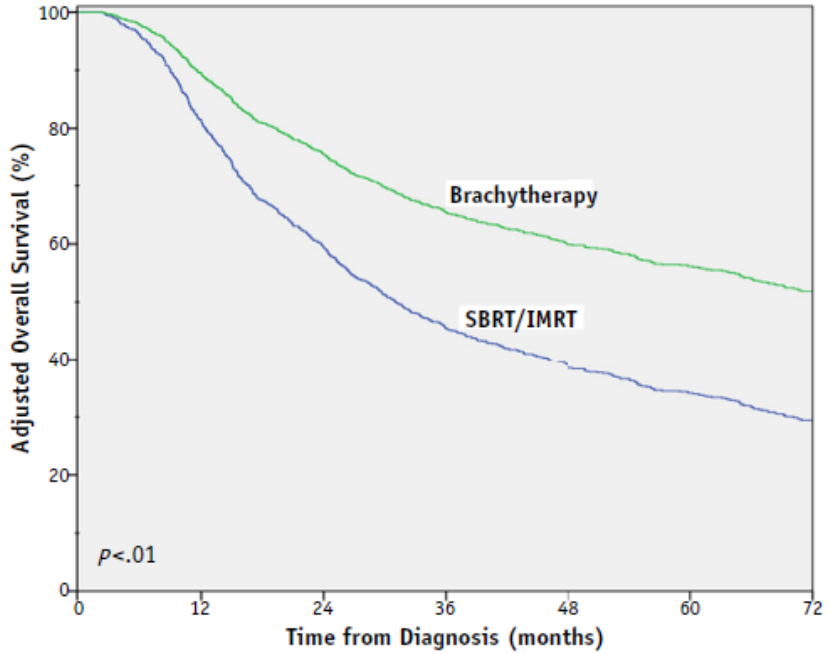


Table 3 Propensity-adjusted multivariable Cox proportional hazards model using parsimonious forward logistic regression

Factor	$HR_{mortality}$	95% CI	*P*
Chemotherapy			
Delivered	1.00	Reference	
Not delivered	1.61	1.27-2.04	<.01*
Boost modality			
Brachytherapy	1.00	Reference	
IMRT or SBRT	1.86	1.35-2.55	<.01*

Gill BS, *et al.* IJROBP 2014

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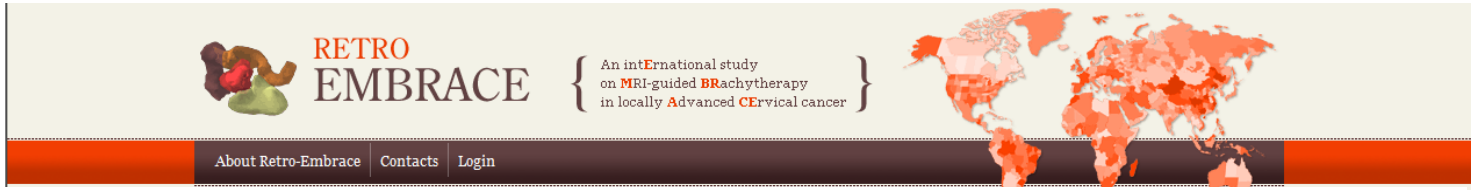
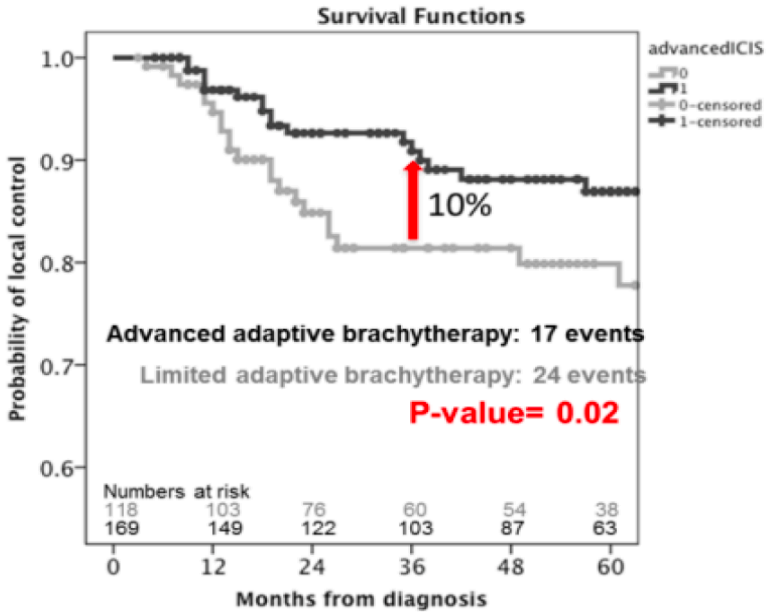
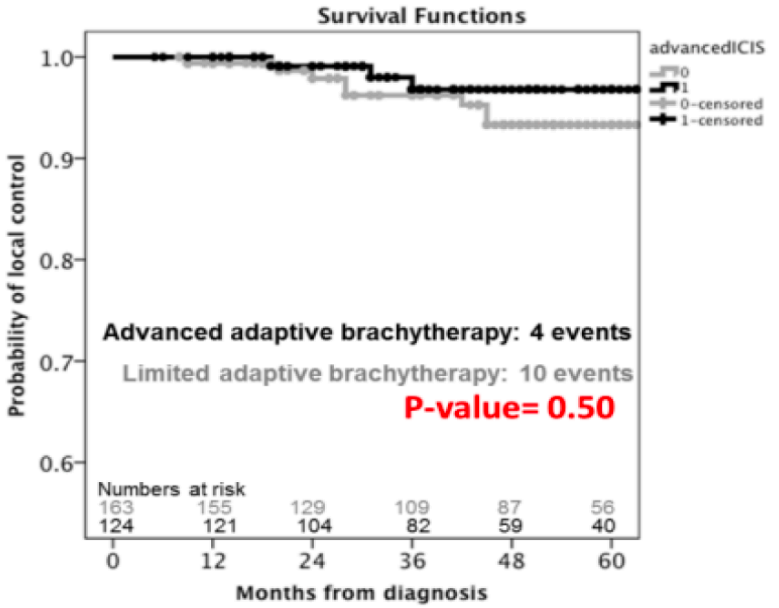
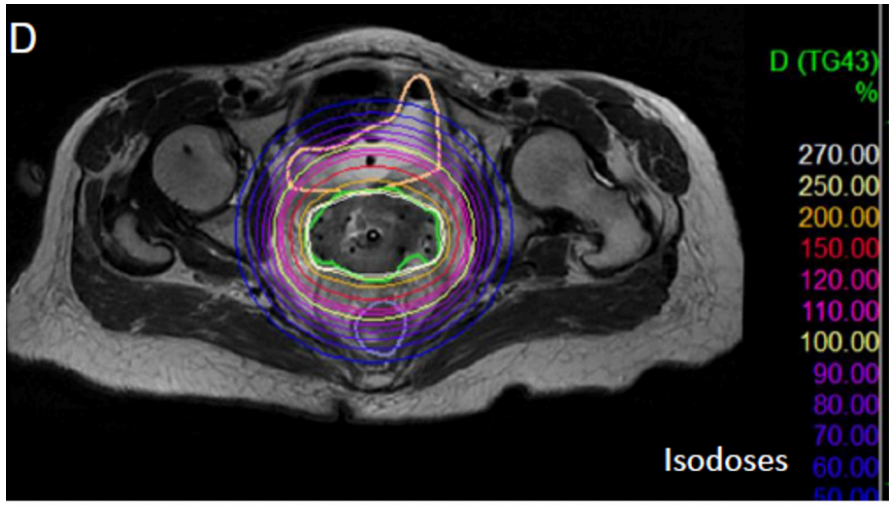


CTVHR $\geq$ 30 cm^3



CTVHR < 30 cm^3





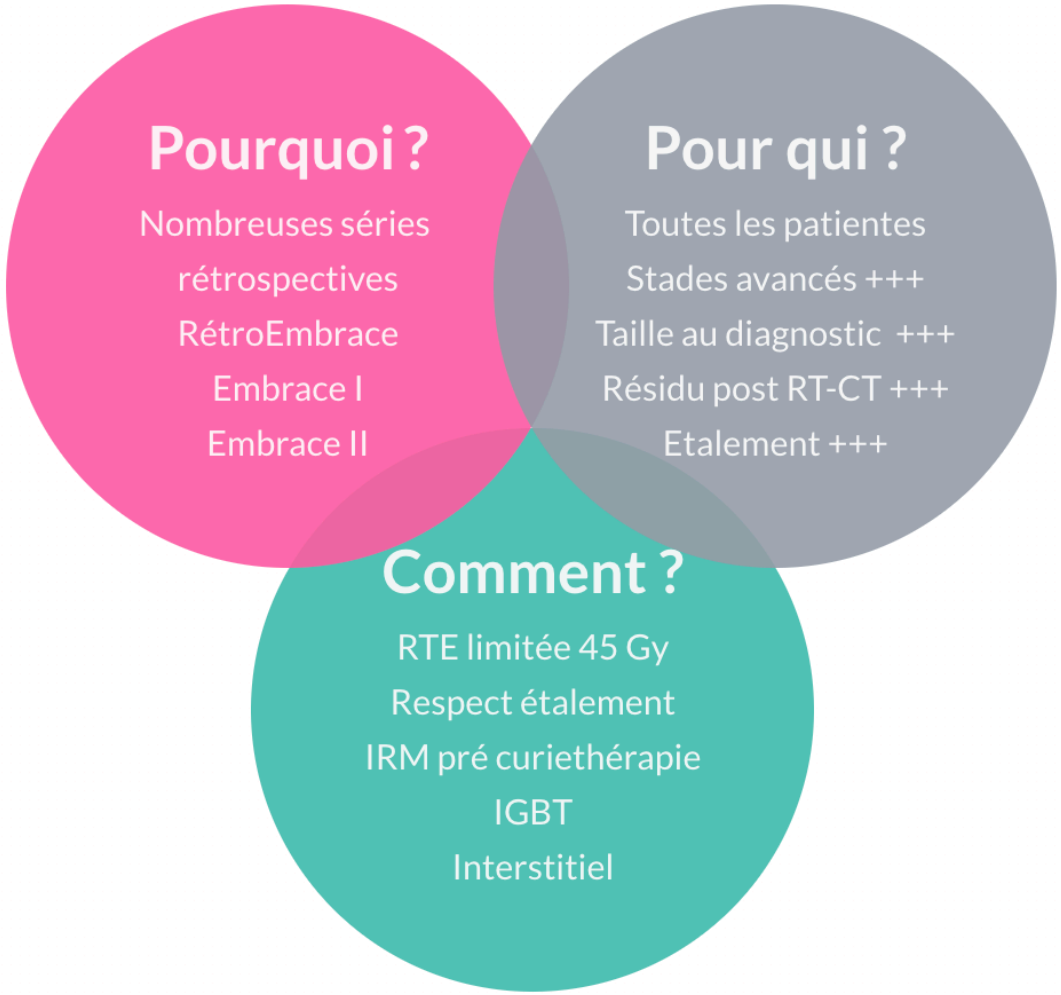
Tanderup *et al.* Radiother Oncol 2016

Conclusion

Standard (col localement avancé) = RT/CT + curiethérapie

- Limiter la dose centro-pelvienne à 45 Gy
- Pas de « boost » en RTE
- Pas de place pour une chirurgie à 45 Gy
- Pas de chirurgie de clôture
- Escalade de dose / **curiethérapie guidée par imagerie** ⇔ contrôle local

Merci !


Pourquoi ?
Nombreuses séries rétrospectives
RétroEmbrace
Embrace I
Embrace II
Pour qui ?
Toutes les patientes
Stades avancés +++
Taille au diagnostic +++
Résidu post RT-CT +++
Etalement +++
Comment ?
RTE limitée 45 Gy
Respect étalement
IRM pré curiethérapie
IGBT
Interstitiel