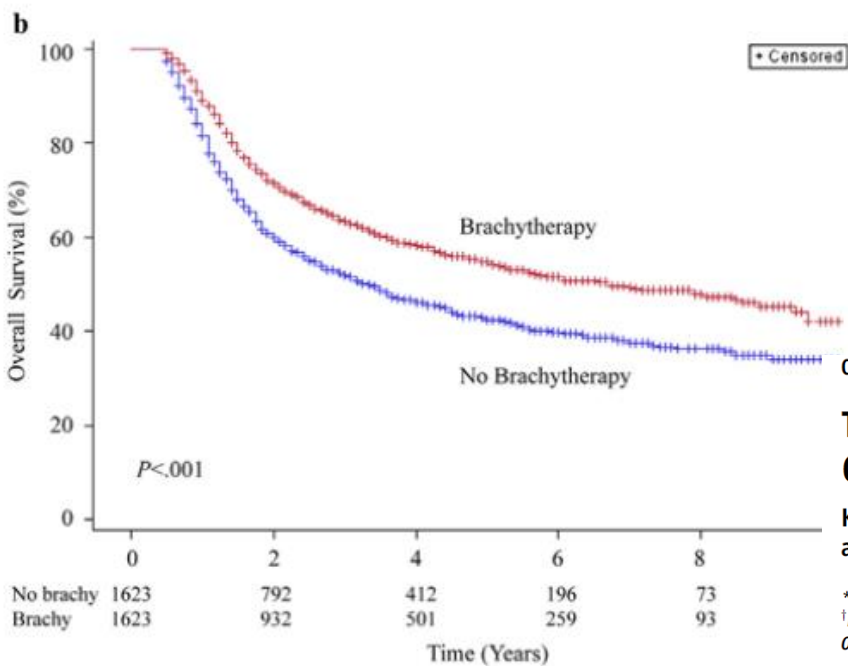
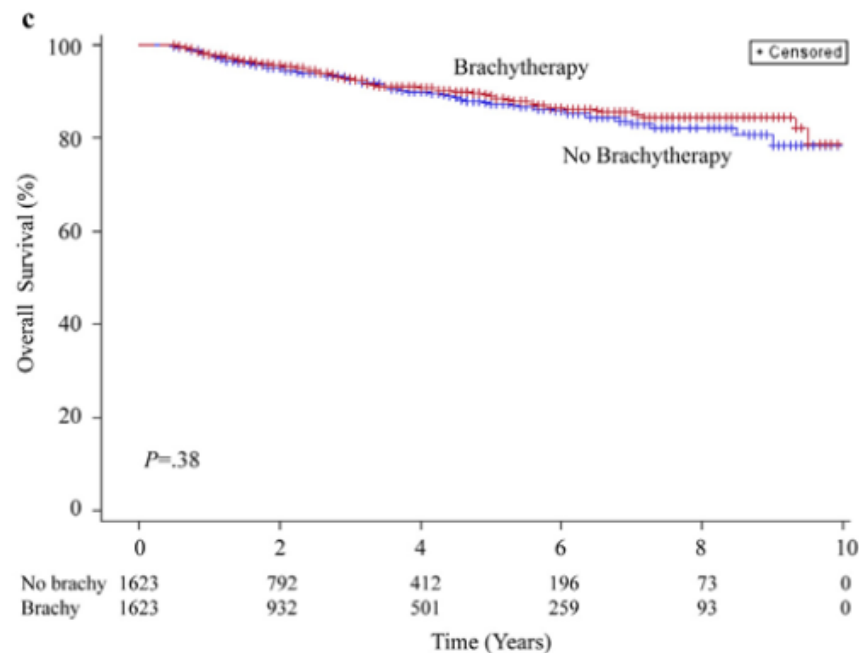
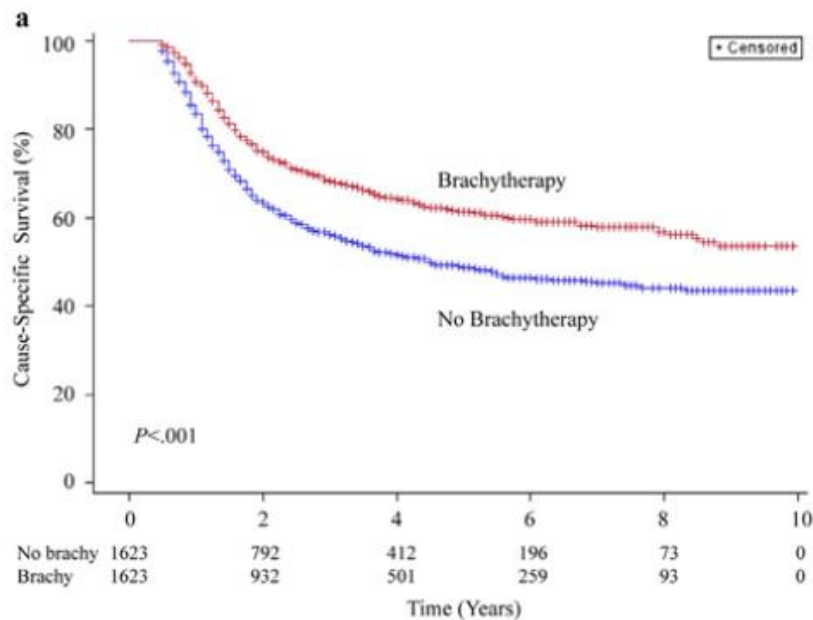


# INNOVATIONS EN RADIOTHÉRAPIE :

D'hier à demain



Curiethérapie guidée par l'image  
Un modèle : le cancer du col



**Fig. 2.** Survival by brachytherapy use for matched cohort between 2000 and 2009. (a) Cause-specific survival; (b) overall survival, and (c) non-cancer-related survival.

Clinical Investigation: Gynecologic Cancer

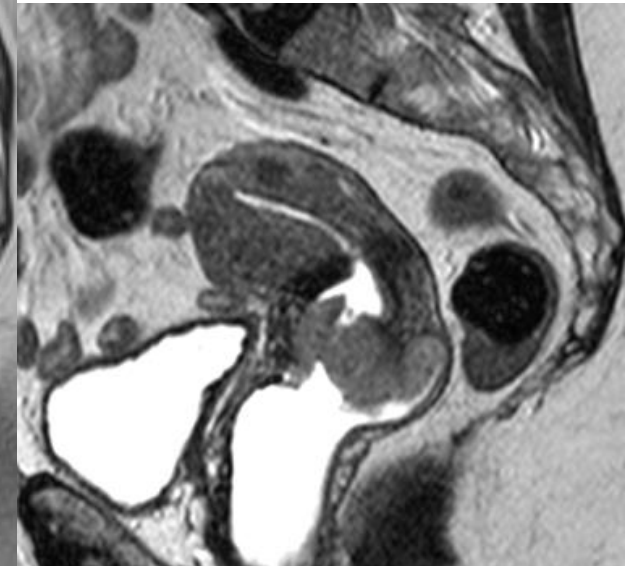
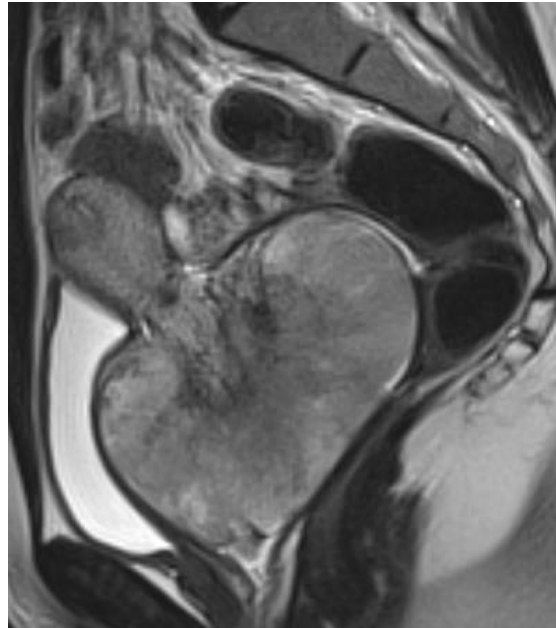
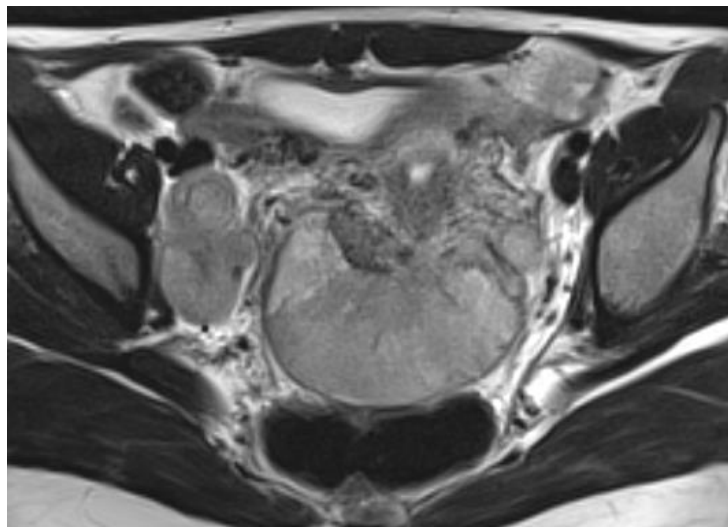
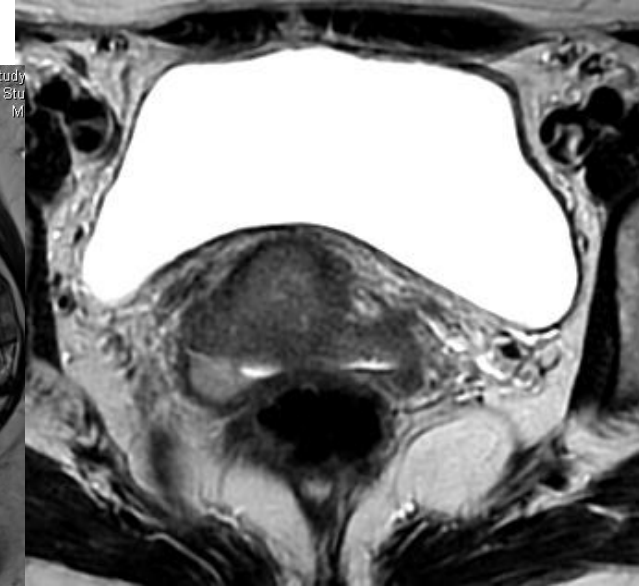
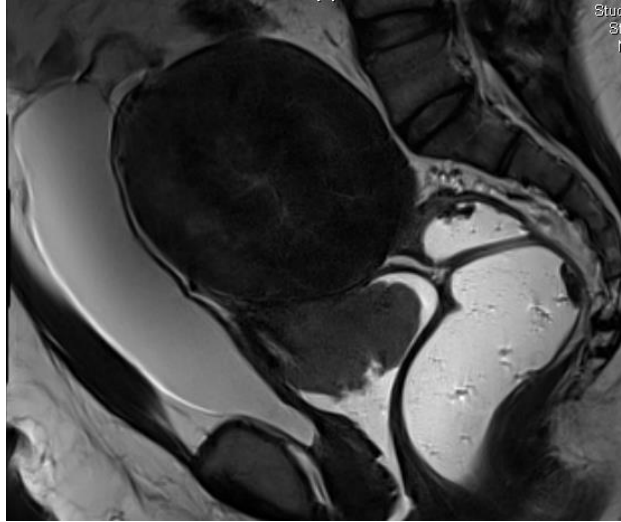
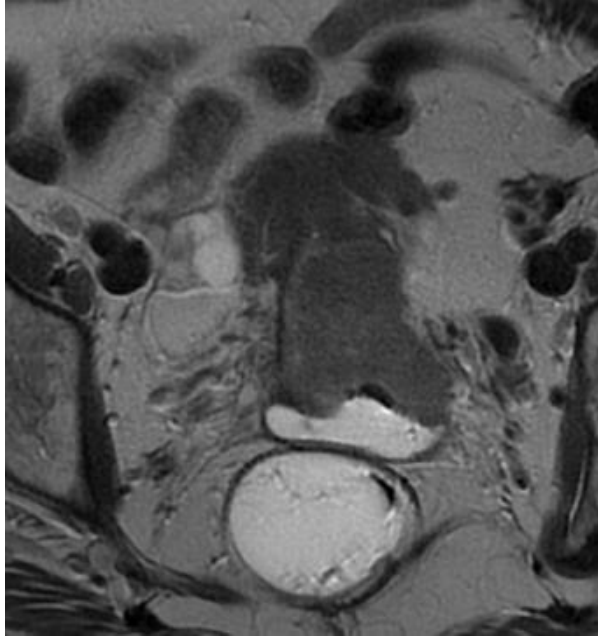
## Trends in the Utilization of Brachytherapy in Cervical Cancer in the United States

Kathy Han, MD,\* Michael Milosevic, MD,\* Anthony Fyles, MD,\* Melania Pintilie, MSc,<sup>†</sup> and Akila N. Viswanathan, MD, MPH<sup>‡</sup>

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# Curiethérapie guidée par l'image dans le cancer du col



# Curiethérapie guidée par l'image dans le cancer du col : recommandations

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.

Haie-Meder C, Pötter R, Van Limbergen E, Briot E, De Brabandere M, Dimopoulos J, Dumas I, Hellebust TP, Kirisits C, Lang S, Muschitz S, Nevinson J, Nulens A, Petrow P, Wachter-Gerstner N; Gynaecological (GYN) GEC-ESTRO Working Group.  
Radiother Oncol. 2005;74:235-45. Review.

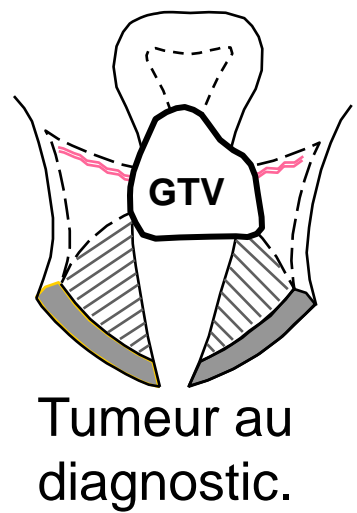
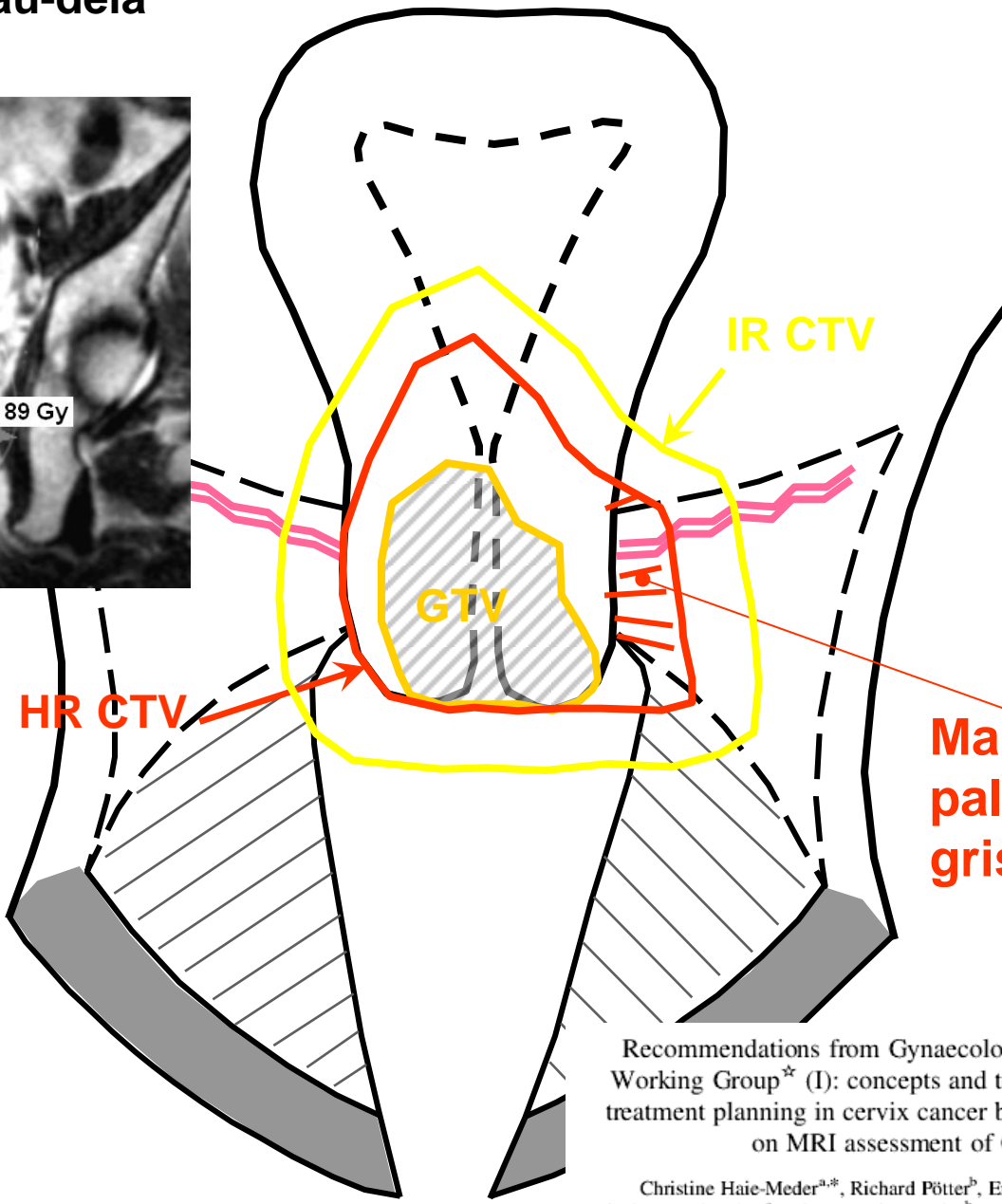
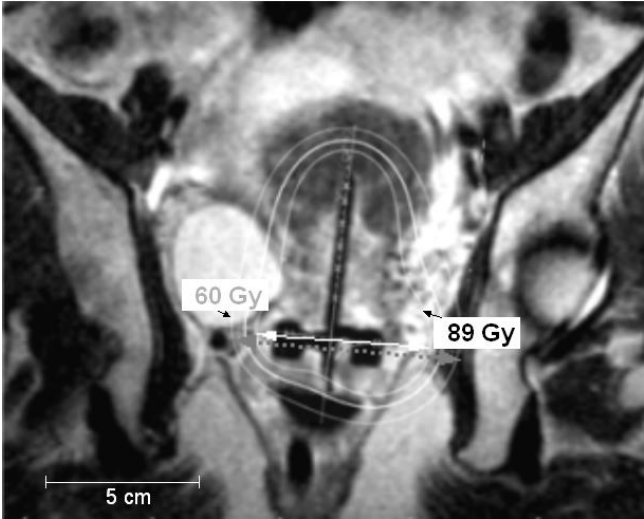
Recommendations from gynaecological (GYN) GEC ESTRO working group (II): concepts and terms in 3D image-based treatment planning in **cervix cancer** brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology.

Pötter R, Haie-Meder C, Van Limbergen E, Barillot I, De Brabandere M, Dimopoulos J, Dumas I, Erickson B, Lang S, Nulens A, Petrow P, Rownd J, Kirisits C; GEC ESTRO Working Group.  
Radiother Oncol. 2006;78:67-77.

Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (IV): Basic principles and parameters for MR imaging within the frame of image based adaptive **cervix cancer** brachytherapy.

Dimopoulos JC, Petrow P, Tanderup K, Petric P, Berger D, Kirisits C, Pedersen EM, van Limbergen E, Haie-Meder C, Pötter R.  
Radiother Oncol. 2012;103:113-22.

maladie étendue au-delà du col (IIB-IVA)

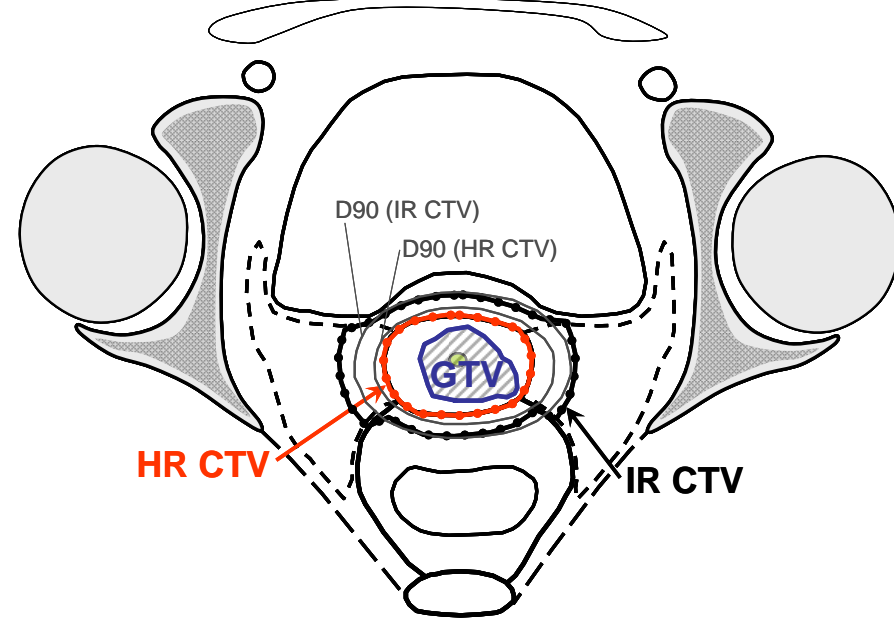
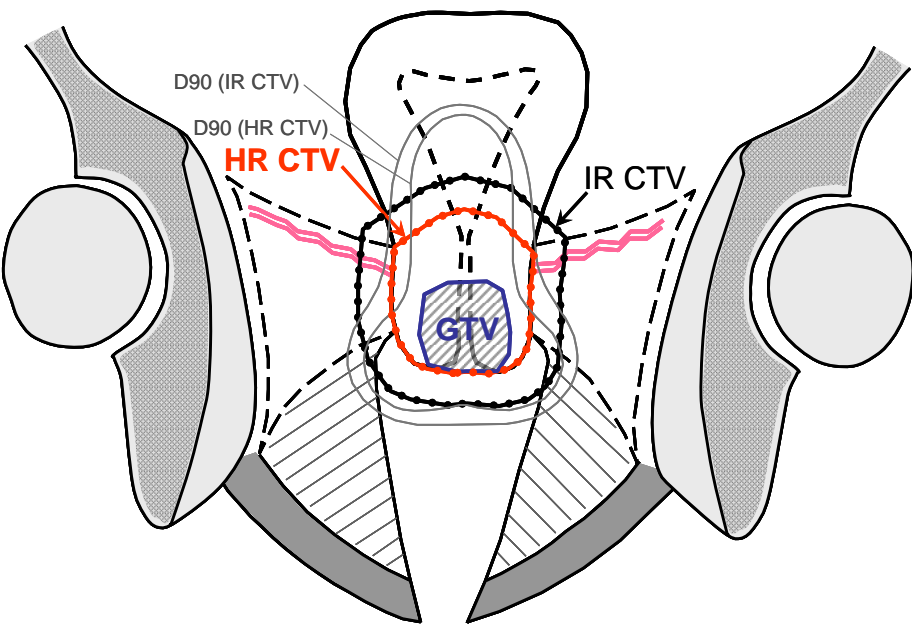


Target Concept for prescription

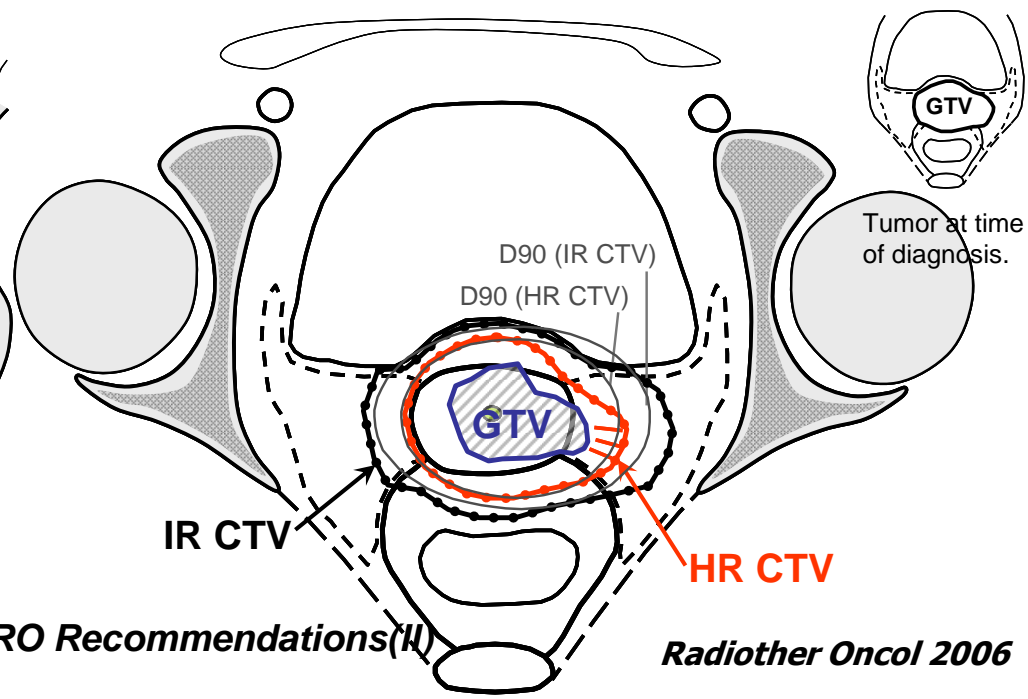
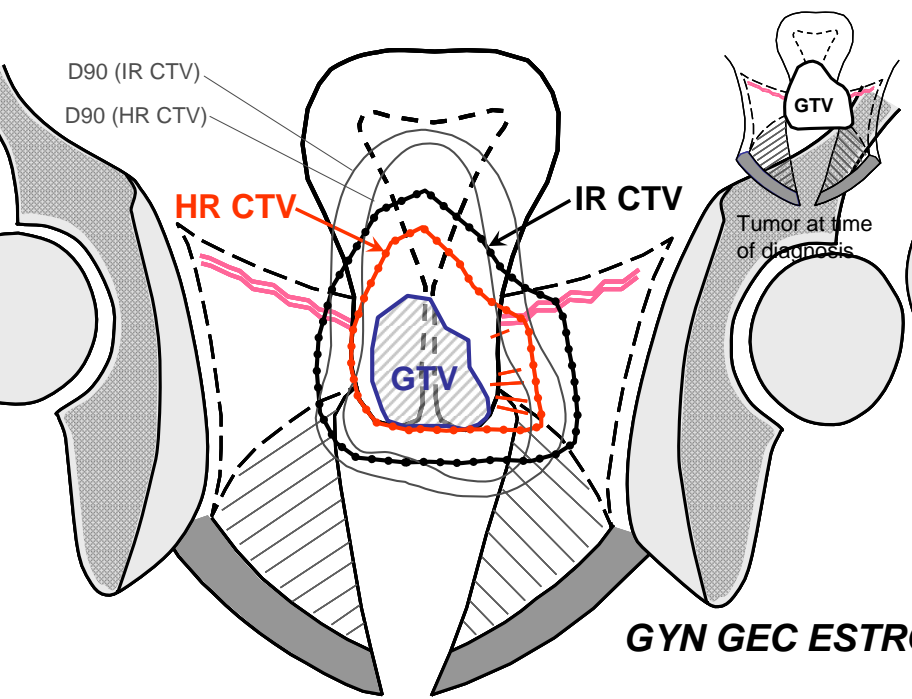
Maladie résiduelle palpable + zones grises (IRM)

Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group<sup>2\*</sup> (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<sup>a,\*</sup>, Richard Pötter<sup>b</sup>, Erik Van Limbergen<sup>c</sup>, Edith Briot<sup>a</sup>, Marisol De Brabandere<sup>c</sup>, Johannes Dimopoulos<sup>b</sup>, Isabelle Dumas<sup>a</sup>, Taran Paulsen Hellebust<sup>d</sup>, Christian Kirisits<sup>b</sup>, Stefan Lang<sup>b</sup>, Sabine Muschitz<sup>b</sup>, Juliana Nevinson<sup>e</sup>, An Nulens<sup>c</sup>, Peter Petrow<sup>f</sup>, Natascha Wachter-Gerstner<sup>b</sup>



## GTV, CTV-HR, CTV-IR et D 90



# Curiethérapie guidée par l'image : Utilisation du modèle linéaire quadratique

## Comparaison:

- modalités curiethérapie
- résultats



A	B	C	D	E	F	G	H	I	J	K	L	M	
$\alpha/\beta$ [Gy]	10		Department of Radiotherapy and Radiobiology, Medical University of Vienna										
$T_{1/2}$ [h]	1,5		Neither the authors nor anybody else can accept any legal responsibility or liability for any errors or omissions that may be made.										
$\mu$ [1/h]	0,46												
<b>EBRT 1</b>		BED	EQD <sub>2</sub>	<b>EBRT 2</b>				BED	EQD <sub>2</sub>	<b>TOTAL EBRT</b>			
		[Gy]	[Gy]				[Gy]	[Gy]			BED	EQD <sub>2</sub>	
number of fractions n	25			number of fractions n							[Gy]	[Gy]	
dose / fraction d [Gy]	1,8	2,1	1,8	dose / fraction d [Gy]		0,0	0,0				[Gy]	[Gy]	
<b>TOTAL</b>	45,0	53,1	44,3	<b>TOTAL</b>	0,0	0,0	0,0			<b>EBRT 1+2</b>	53,1	44,3	
<b>PDR 1</b>		BED	EQD <sub>2</sub>	<b>PDR 2</b>				BED	EQD <sub>2</sub>	<b>TOTAL PDR</b>			
		[Gy]	[Gy]				[Gy]	[Gy]			BED	EQD <sub>2</sub>	
pulse dose $d_{p,1}$ [Gy]	0,8			pulse dose $d_{p,2}$ [Gy]							[Gy]	[Gy]	
number of pulses $n_1$	50			number of pulses $n_2$							[Gy]	[Gy]	
pulse repetition time [h]	1			pulse repetition time [h]							[Gy]	[Gy]	
pulse irradiation time $t_1$ [h]	0,5			pulse irradiation time $t_2$ [h]							[Gy]	[Gy]	
dose fraction 1 $d_1$ [Gy]	40,0	53,3	44,4	dose fraction 2 $d_2$ [Gy]	0,0	0,0	0,0			<b>PDR 1+2</b>	53,3	44,4	
											<b>TOTAL EBRT + PDR</b>		
											BED	EQD <sub>2</sub>	
											[Gy]	[Gy]	
											<b>EBRT + PDR</b>	106,4	88,7

# Curiethérapie guidée par l'image : Utilisation du modèle linéaire quadratique

## Comparaison:

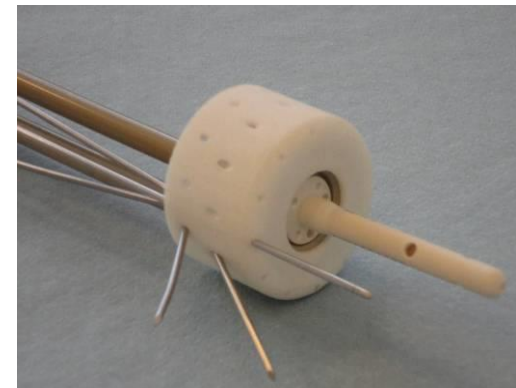
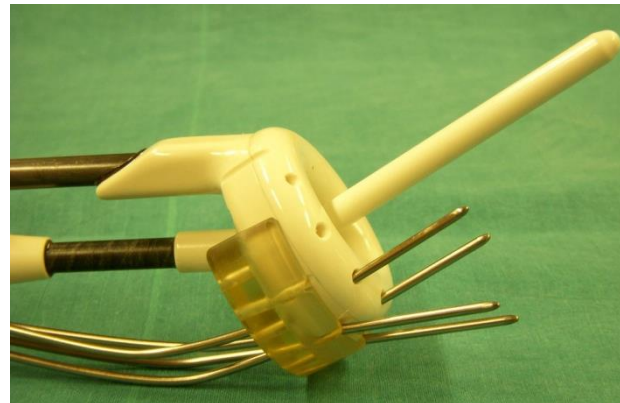
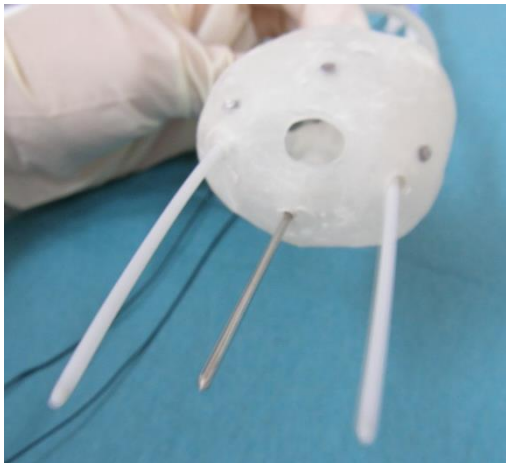
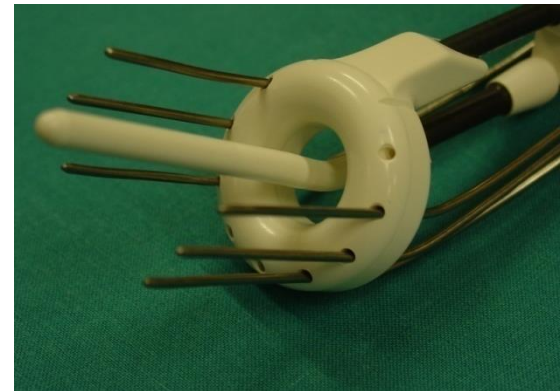
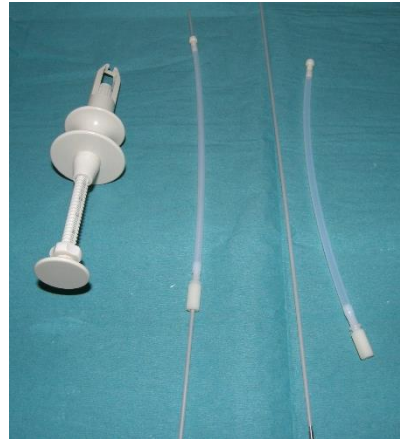
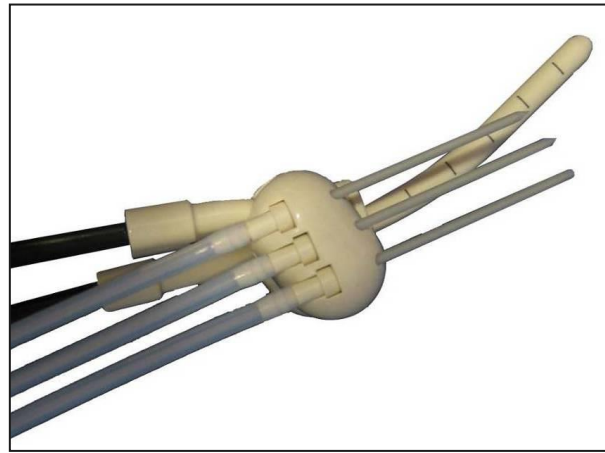
- modalités curiethérapie
- résultats



A	B	C	D	E	F	G	H	I	J	K	L	M	
$\alpha/\beta$ [Gy]	3		Department of Radiotherapy and Radiobiology, Medical University of Vienna										
$T_{1/2}$ [h]	1,5		Neither the authors nor anybody else can accept any legal responsibility or liability for any errors or omissions that may be made.										
$\mu$ [1/h]	0,46												
<b>EBRT 1</b>		BED	EQD <sub>2</sub>	<b>EBRT 2</b>				BED	EQD <sub>2</sub>	<b>TOTAL EBRT</b>			
		[Gy]	[Gy]				[Gy]	[Gy]					
number of fractions n	25			number of fractions n							BED	EQD <sub>2</sub>	
dose / fraction d [Gy]	1,8	2,9	1,7	dose / fraction d [Gy]			0,0	0,0			[Gy]	[Gy]	
<b>TOTAL</b>	45,0	72,0	43,2	<b>TOTAL</b>	0,0		0,0	0,0			<b>EBRT 1+2</b>	72,0	43,2
<b>PDR 1</b>		BED	EQD <sub>2</sub>	<b>PDR 2</b>				BED	EQD <sub>2</sub>	<b>TOTAL PDR</b>			
		[Gy]	[Gy]				[Gy]	[Gy]					
pulse dose $d_{p,1}$ [Gy]	0,8			pulse dose $d_{p,2}$ [Gy]									
number of pulses $n_1$	50			number of pulses $n_2$									
pulse repetition time [h]	1			pulse repetition time [h]									
pulse irradiation time $t_1$ [h]	0,5			pulse irradiation time $t_2$ [h]									
dose fraction 1 $d_1$ [Gy]	40,0	84,4	50,6	dose fraction 2 $d_2$ [Gy]	0,0		0,0	0,0			<b>PDR 1+2</b>	84,4	50,6
<b>TOTAL EBRT + PDR</b>													
											BED	EQD <sub>2</sub>	
											[Gy]	[Gy]	
											<b>EBRT + PDR</b>	156,4	93,8

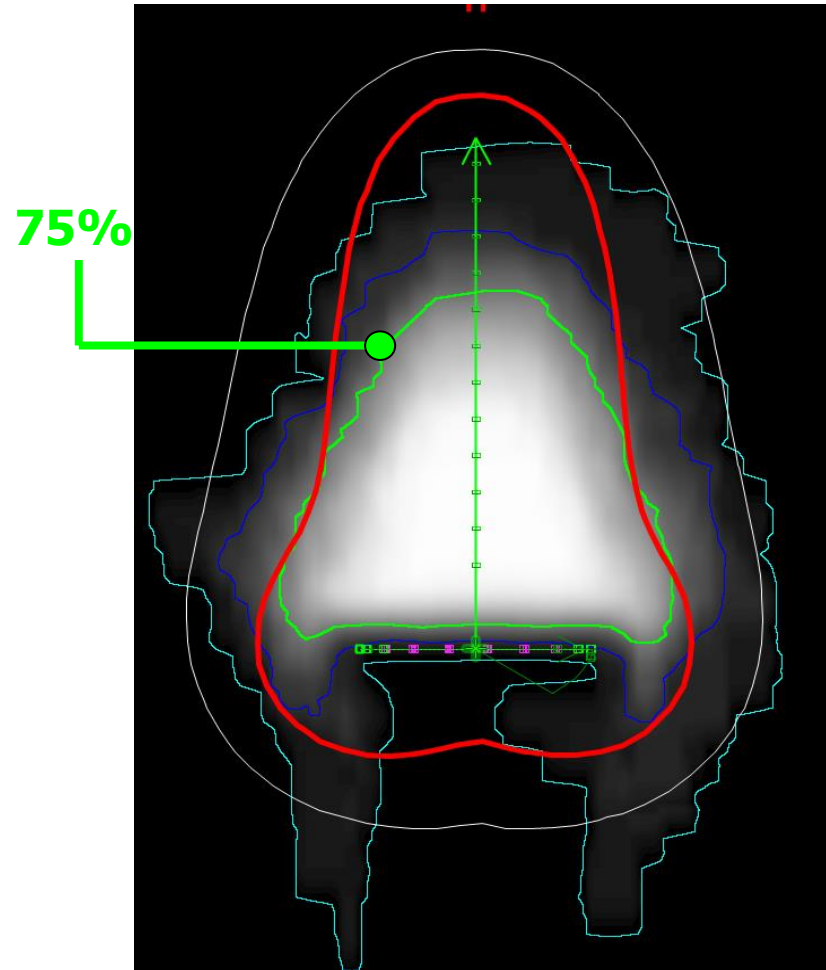
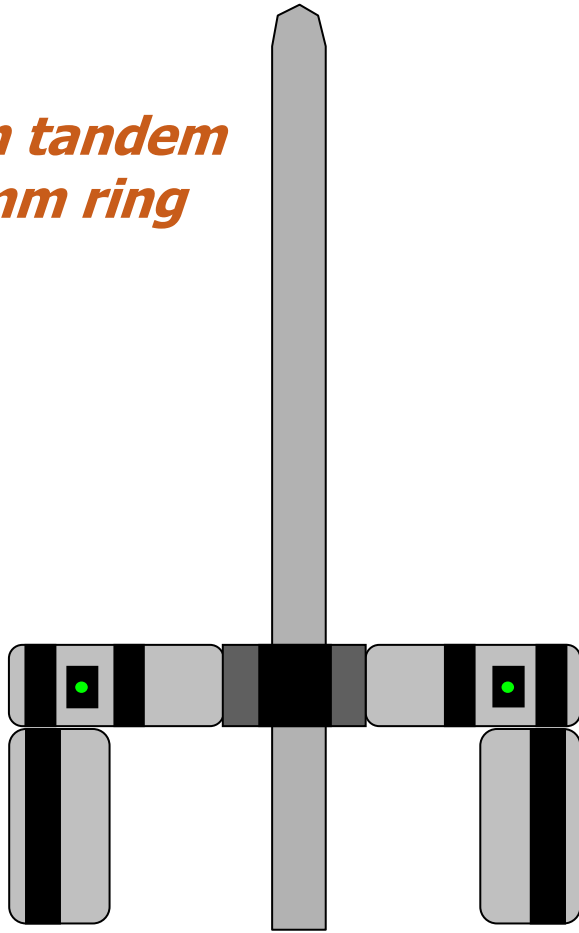


# Curiethérapie guidée par l'image : Développement des techniques de curiethérapie interstitielle



# Curiethérapie guidée par l'image : Fréquence curiethérapie interstitielle

- *6 cm tandem*
- *30 mm ring*



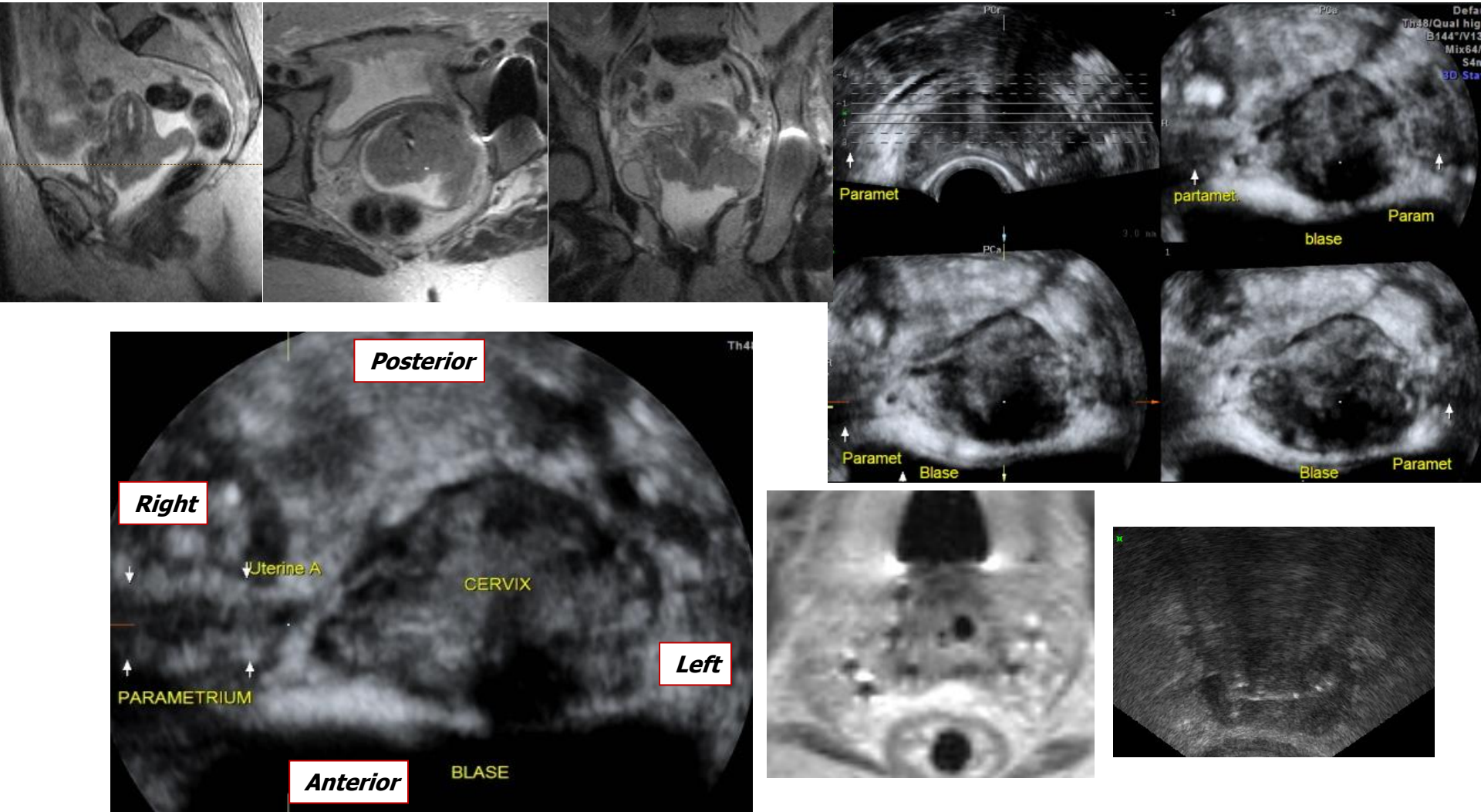
# Curiethérapie guidée par l'image : études

- Réponse à l'irradiation
- Alternative à l'IRM
- Optimisation
- Contraintes aux OAR
- Résultats cliniques

# Curiethérapie guidée par l'image : Régression tumorale pendant RTE + chimio

<b>Study</b>	<b>Pt nb</b>	<b>Tumor definition</b>	<b>Tumor regression after 45-50Gy</b>
<b>Hatano</b>	<b>42</b>	<b>High SI</b>	<b>71%</b>
<b>Lim</b>	<b>27</b>	<b>High SI</b>	<b>74%</b>
<b>Chargari</b>	<b>45</b>	<b>HR-CTV</b>	<b>45%</b>
<b>Dimopoulos</b>	<b>49</b>	<b>High SI+GZ</b>	<b>75%</b>
<b>Haie-Meder</b>	<b>84</b>	<b>HR-CTV</b>	<b>65%</b>
<b>Schmid</b>	<b>175</b>	<b>High SI</b>	<b>78.5%</b>
		<b>High SI+GZ</b>	<b>50.1%</b>

# Curiethérapie guidée par l'image Alternative à l'IRM?



# Curiethérapie guidée par l'image : Homogénéisation des pratiques

Radiotherapy and Oncology 94 (2010) 339–345



Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: [www.thegreenjournal.com](http://www.thegreenjournal.com)



Cervix cancer brachytherapy

Variation of treatment planning parameters ( $D_{90}$  HR-CTV,  $D_{2cc}$  for OAR) for cervical cancer tandem ring brachytherapy in a multicentre setting: Comparison of standard planning and 3D image guided optimisation based on a joint protocol for dose–volume constraints

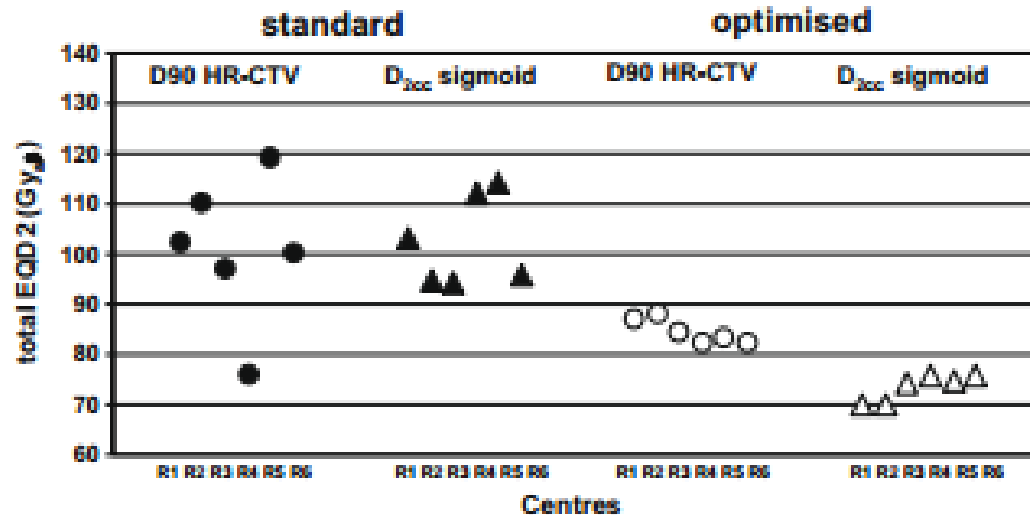
Ina M. Jürgenliemk-Schulz <sup>a,1</sup>, Stefan Lang <sup>b,\*,1</sup>, Kari Tanderup <sup>c</sup>, Astrid de Leeuw <sup>a</sup>, Christian Kirisits <sup>b</sup>, Jacob Lindegaard <sup>c</sup>, Primoz Petric <sup>d</sup>, Robert Hudej <sup>d</sup>, Richard Pötter <sup>b</sup>, On behalf of the Gyn GEC ESTRO network

**Table 1**

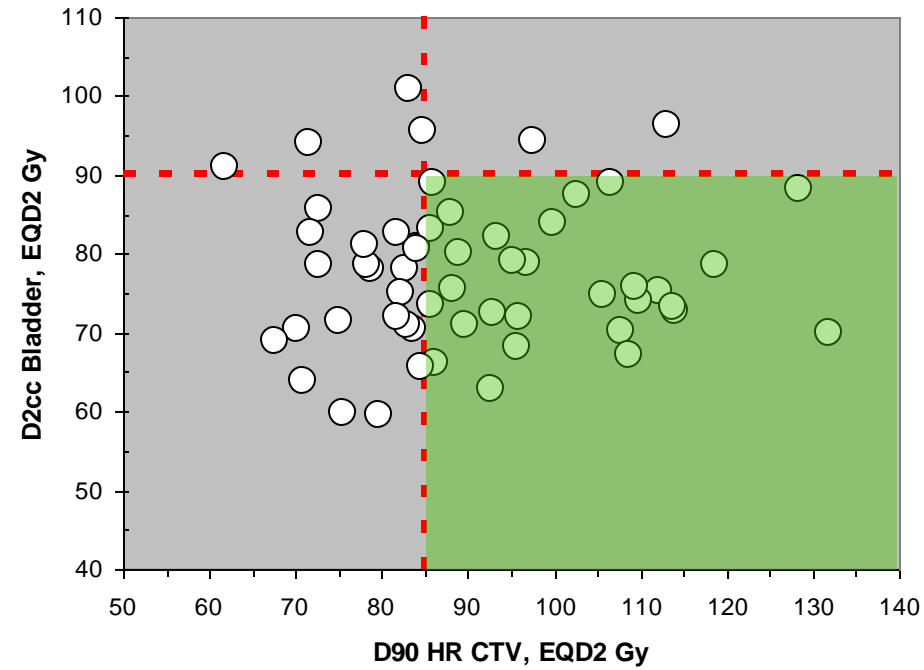
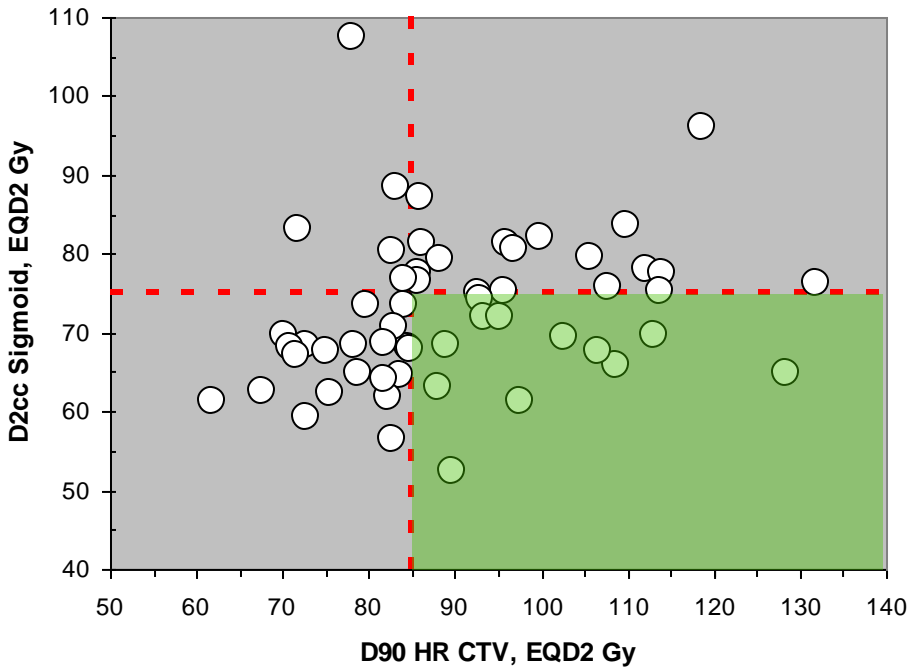
Treatment concepts of the different ring centres (R1–R6): EBRT dose, BT dose rate and fractionation schedule, additional interstitial sources.

Centre	R1	R2	R3	R4	R5	R6
<b>EBRT</b>						
Physical dose (Gy)	45	45	45	45	45	45
Fractionation	25 × 1.8	25 × 1.8	25 × 1.8	25 × 1.8	25 × 1.8	25 × 1.8
<b>Brachytherapy</b>						
Dose rate	PDR	PDR	HDR	HDR	HDR	HDR
Number of fractions	3	2	6	5	4	3
Prescribed physical dose/fraction (Gy)	12	20	4.7	5.5	7	7
Interstitial needles	Yes	Yes	No	No	Yes	No

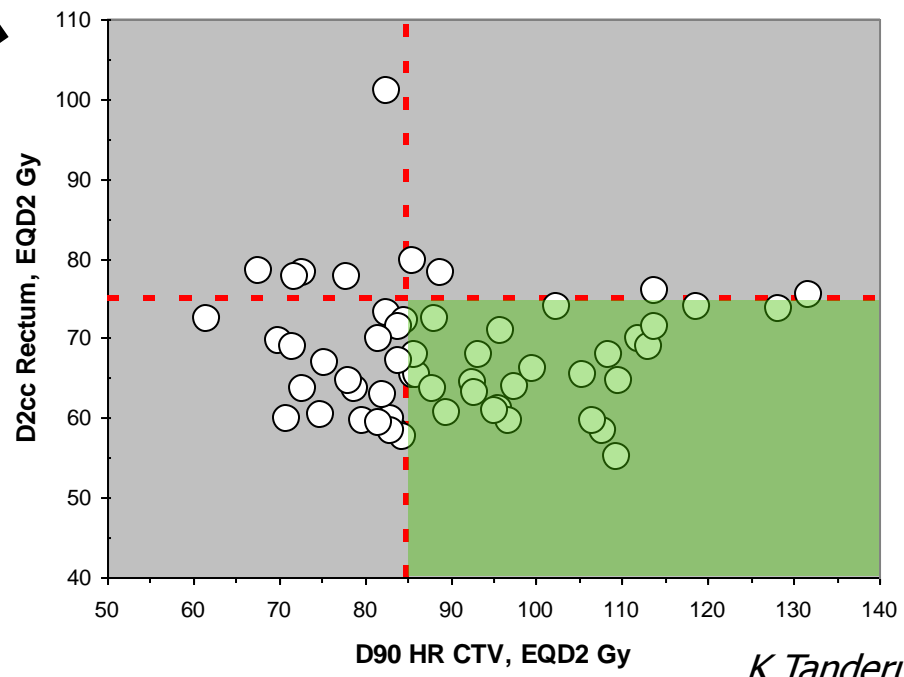
# Curiothérapie guidée par l'image : Homogénéisation des pratiques



**Fig. 2.** Dose level variations (D90 HR-CTV and D<sub>2cc</sub> sigmoid) in standard and optimised plans from the different centres for the limited volume case. The radiobiological effect of dose rate (PDR: R1/R2, HDR: R3/R4/R5/R6) and fractionation is indicated for the different treatment schedules (3rd and 4th column). Number of fractions is decreasing and dose per fraction is increasing for R3–R6 (compare Table 1).

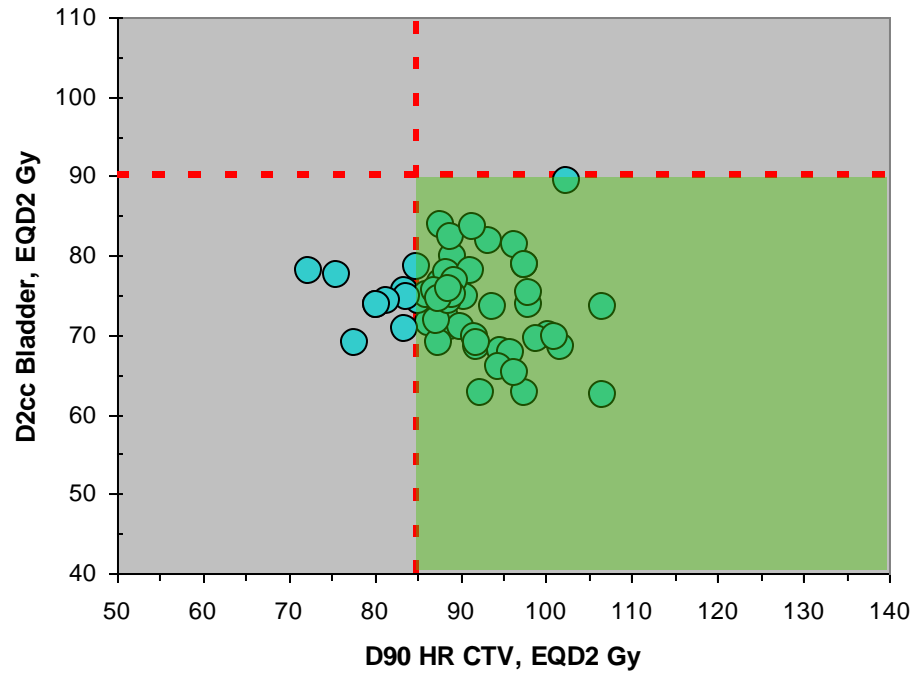
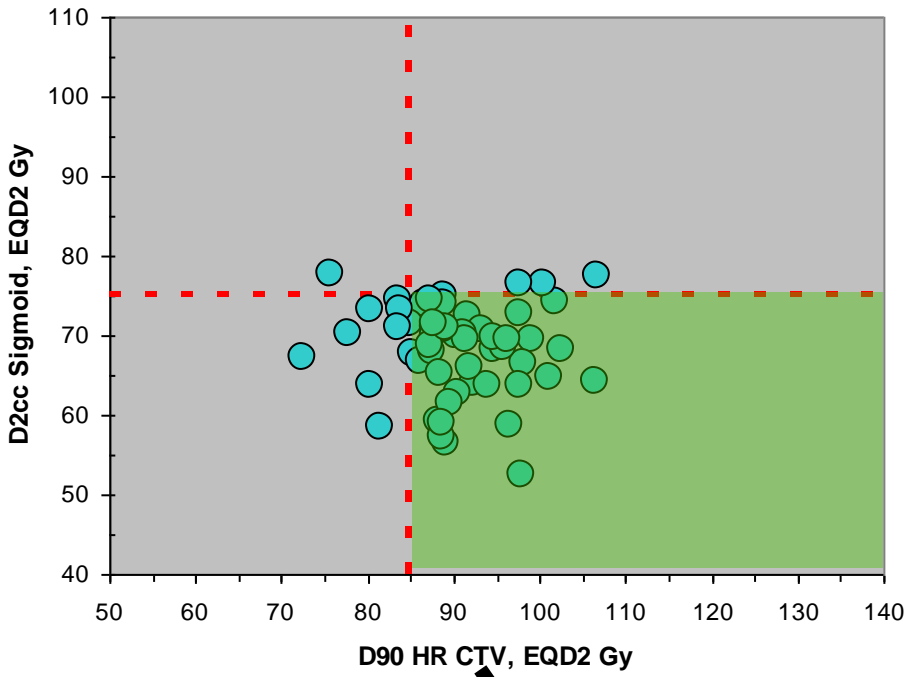


**2D standard  
plans**

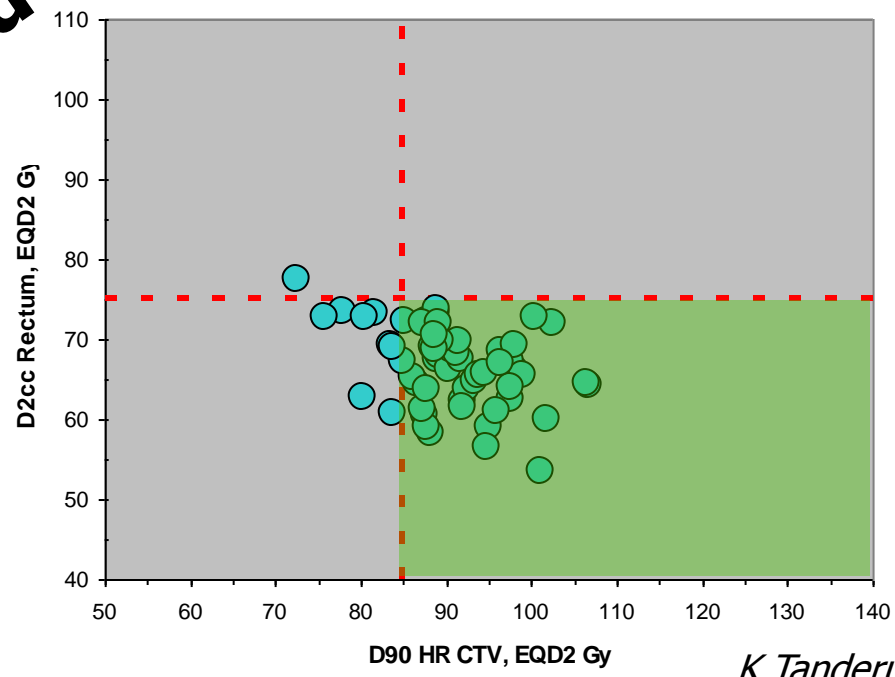


10/57 pts





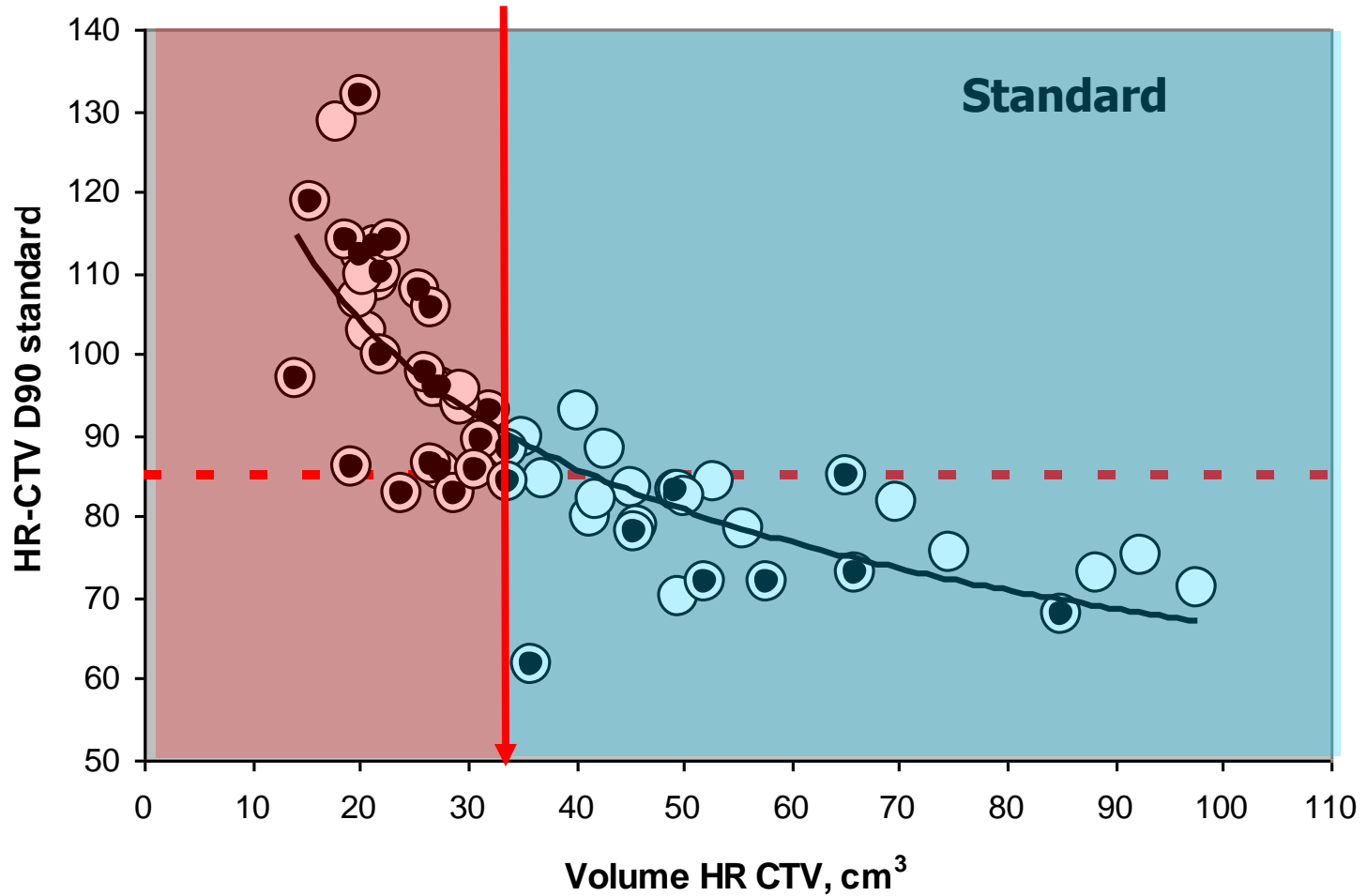
**3D optimised plans**



**44/57 pts**

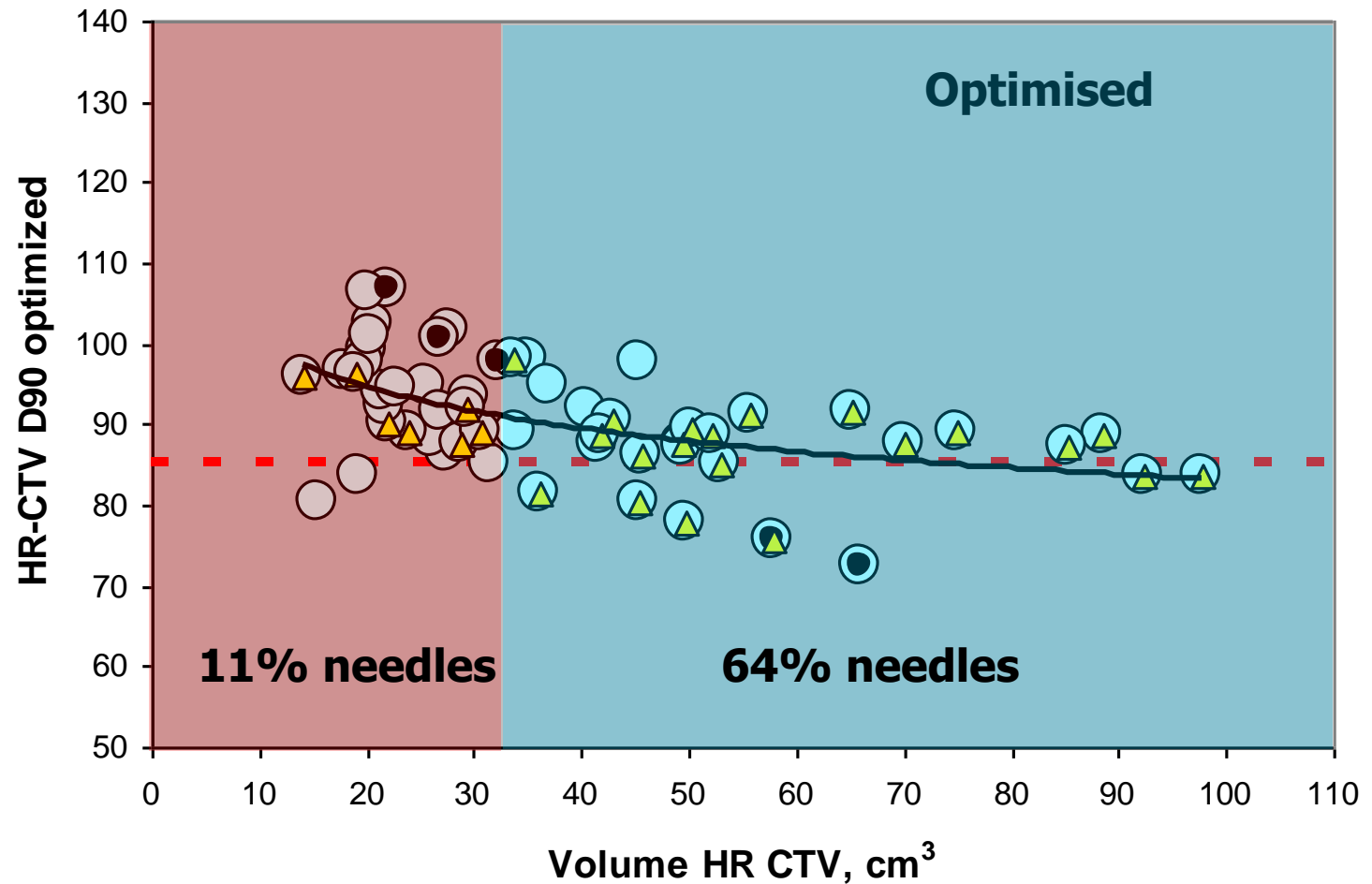
Volume médian : 32cm<sup>3</sup>

# Importance du volume



● Violation of OAR constraint

# Importance du volume



● Violation of OAR constraint

▲ Application of needles

# Bénéfice de l'optimisation

Pourcentage de patientes avec respect des contraintes HDV

	Tumeurs < 32cm <sup>3</sup>		Tumeurs ≥ 32cm <sup>3</sup>	
	STANDARD	OPTIMISED	STANDARD	OPTIMISED
<b>Couverture CTV-HR</b>	<b>93%</b>	<b>93%</b>	<b>14%</b>	<b>71%</b>
<b>Respect OAR</b>	<b>24%</b>	<b>90%</b>	<b>64%</b>	<b>93%</b>

# Curiethérapie guidée par l'image :

## Résultats mono-institutionnels

Author	Pt nb	image modal.	BT modal.	Total EQD2 D90 HR-CTV	Local control
Chargari 2009	45	MRI	PDR	75	100%
Haie-Meder 2009	39	MRI	LDR	60*	94%
Haie-Meder 2010	84	MRI	LDR	79	90%
Beriwal 2011	44	Hybrid	HDR	83	88%
Potter 2011	156	MRI	HDR	93	97%
Lindegaard 2013	140	MRI	PDR	91	90%
Mazon 2013	163	MRI	PDR	78	95%
Nomden 2013	46	MRI	PDR/HDR	84	93%
Refaat 2013	40	MRI	PDR	±80	90%
Tharavichitkul 2013	47	MRI/CT	HDR	93	98%
Rijkmans 2014	126:				
	43 CBT		LDR		83,7%
	83 IGBT	MRI	HDR	80,8	98,8%



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## Radiotherapy and Oncology

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Prospective trial in 3D PDR brachytherapy

Impact of 3D image-based PDR brachytherapy on outcome of patients treated for cervix carcinoma in France: Results of the French STIC prospective study <sup>☆</sup>Claire Charra-Brunaud <sup>a,\*</sup>, Valentin Harter <sup>a</sup>, Martine Delannes <sup>g</sup>, Christine Haie-Meder <sup>c</sup>, Philippe Quetin <sup>d</sup>, Christine Kerr <sup>e</sup>, Bernard Castelain <sup>f</sup>, Laurence Thomas <sup>b</sup>, Didier Peiffert <sup>a</sup>**Table 1**

Comparison of main clinical factors between 2D and 3D arms.

	Group 1 BT followed by surgery		Group 2 EBRT BT surgery		Group 3 EBRT BT		<i>p</i> <sup>*</sup>
	2D	3D	2D	3D	2D	3D	
Number of patients	76	89	142	163	118	117	
Mean age	47.6	46.6	49	47.6	56.1	53.4	0.07
Histology							0.08
Squamous cell	50 (66%)	60 (67%)	120 (84%)	123 (75%)	106 (90%)	99 (85%)	
Adenocarcinoma	22 (29%)	26 (29%)	21 (15%)	38 (23%)	12 (10%)	17 (14%)	
Other	4 (5%)	3 (4%)	1 (1%)	2 (2%)	0	1 (1%)	
FIGO stage							0.27
IB1	66 (87%)	83 (93%)	13 (9%)	16 (10%)	6 (5%)	11 (9%)	
IB2 IIA IIB	10 (13%)	6 (7%)	118 (83%)	127 (78%)	70 (59%)	77 (66%)	
IIIA IIIB	0 (0%)	0 (0%)	11 (8%)	20 (12%)	42 (36%)	29 (25%)	
Mean tumor maximal size (mm)	23 ± 9	28 ± 13	46 ± 16	46 ± 14	49 ± 16	48.5 ± 16	0.44
Pelvic node <sup>1</sup>	3 (4%)	2 (2%)	45 (32%)	63 (39%)	52 (44%)	54 (46%)	0.34
LomboAortic node <sup>1</sup>	0	0	16 (11%)	16 (10%)	22 (19%)	17 (15%)	0.33

<sup>1</sup> nodes diagnosed on imagery (CT/MRI/ or PET CT).<sup>\*</sup> 2D–3D brachytherapy comparison: Generalized Estimated Equations adapted for nested analysis.

Prospective trial in 3D PDR brachytherapy

## Impact of 3D image-based PDR brachytherapy on outcome of patients treated for cervix carcinoma in France: Results of the French STIC prospective study <sup>☆</sup>

Claire Charra-Brunaud <sup>a,\*</sup>, Valentin Harter <sup>a</sup>, Martine Delannes <sup>g</sup>, Christine Haie-Meder <sup>c</sup>, Philippe Quetin <sup>d</sup>, Christine Kerr <sup>e</sup>, Bernard Castelain <sup>f</sup>, Laurence Thomas <sup>b</sup>, Didier Peiffert <sup>a</sup>

**Table 5**  
Clinical results at 24 months.

At 24 months	Group 1 (%)		Group 2 (%)		Group 3 (%)		P*
	2D	3D	2D	3D	2D	3D	
LFRS	91.9	100	84.7	93	73.9	78.5	0.003
RLRFS	87.9	96.1	77.2	88.6	61.2	69.6	0.001
DFS	86.5	89.7	73	77.1	55.2	60.3	0.086
OS	95	96	85	86	65	74	0.27
Grade 3–4 toxicity							
Urinary	5.8	1.3	7.6	5.5	9.2	1.2	0.02
Digestive	6.8	1.2	0.9	4.8	9	0	0.17
Urinary + digestive	9.9	2.5	7.8	9	13.8	1.2	0.027
Gynecologic	5.7	7.5	6.4	2.8	15.4	1.4	0.01
Global	14.6	8.9	12.5	8.8	22.7	2.6	0.002
Grade 2–4 toxicity							
Urinary	13.1	7.9	20.4	13.3	23.1	13.7	0.03
Digestive	8.3	7.4	8.3	8.8	18.7	15.2	0.45
Gynecologic	18.7	12.9	17.9	14.7	35.7	19.4	0.125
Global	37.5	23.2	40.6	29.4	53.4	42.4	0.028

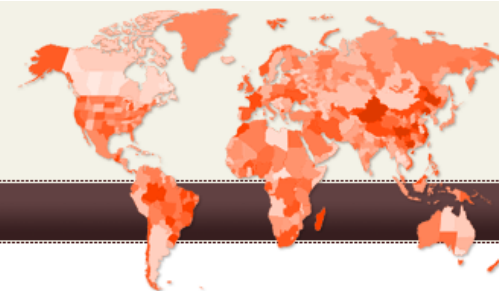
LFRS: local free relapse survival; RLRFS: loco regional relapse free survival; DFS: disease free survival; OS: Overall Survival.

\* 2D-3D brachytherapy comparison: Cox proportional hazard model adjusted for regimens.



**RETRO  
EMBRACE**

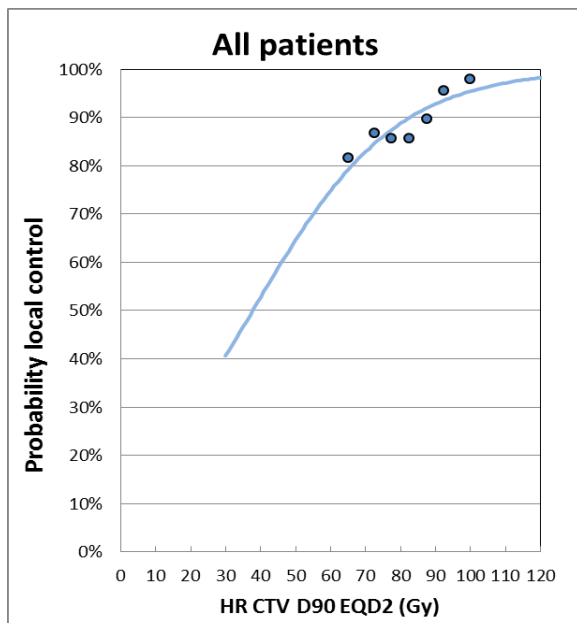
{ An international study  
on MRI-guided BRachytherapy  
in locally Advanced CErvical cancer }



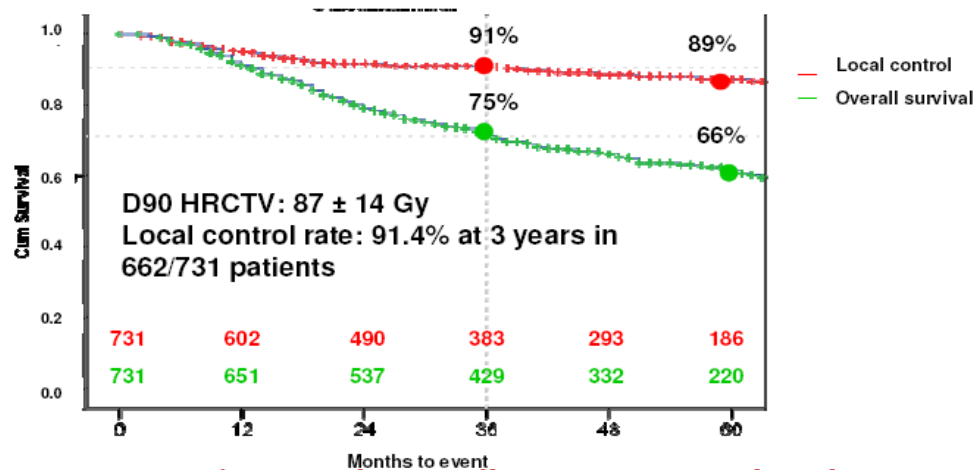
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Sturza 2013

- Multicentric retrospective study
- Concomitant chemoradiation and MRI-IGABT
- GEC-ESTRO recommendations
- 731 patients / 12 institutions



### Actuarial LC and OS on 731 patients

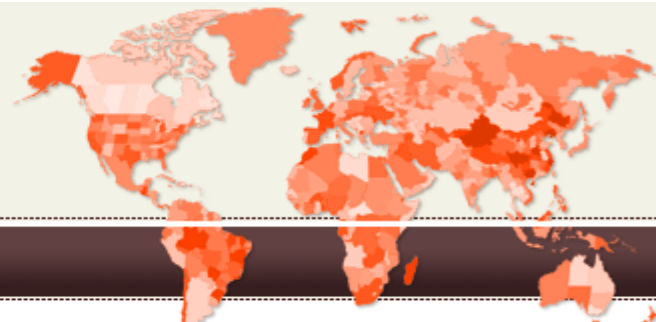






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## 24 Active Centers

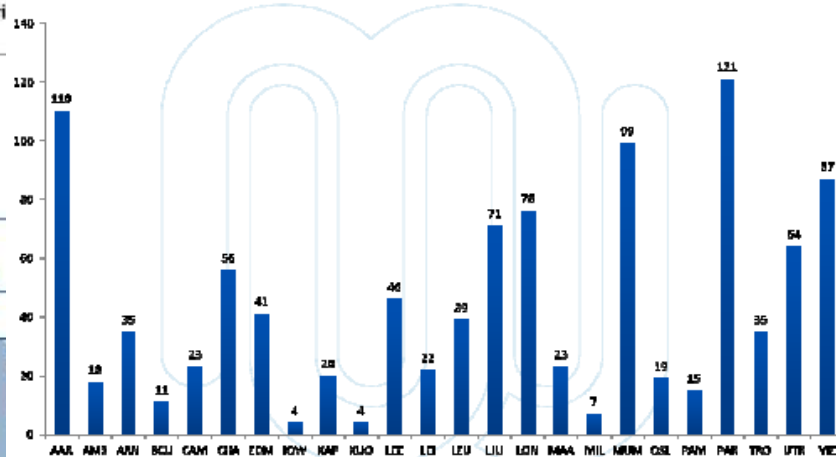
30 centers pass  
27 centers get to  
24 centers contri



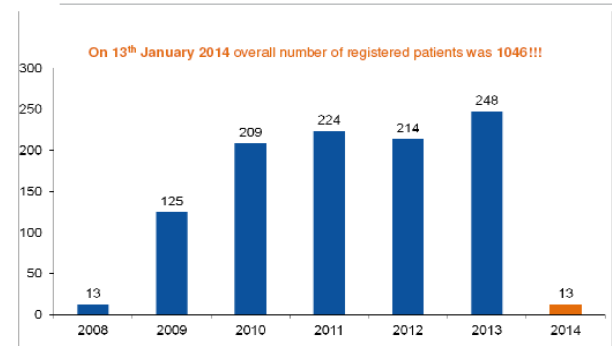
Mumbai  
Chandigarh



## Center Overall Accrual



## Overall Accrual



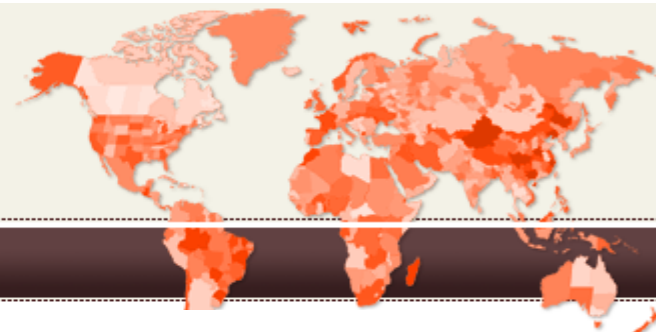
- Vienna
- Aarhus
- Utrecht
- Leiden
- Leuven
- Ljubljana
- London
- Arnhem
- Pamplona
- Paris
- Kaposvar
- Maastricht
- Trondheim
- Leeds
- Oslo
- Amsterdam
- Kuopio
- Cambridge





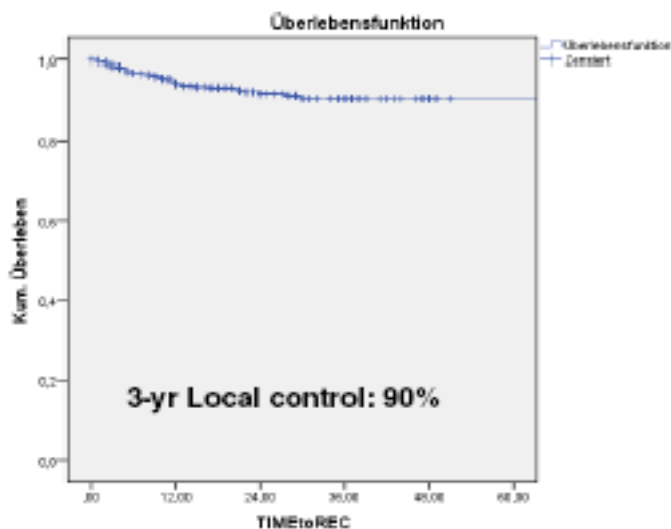
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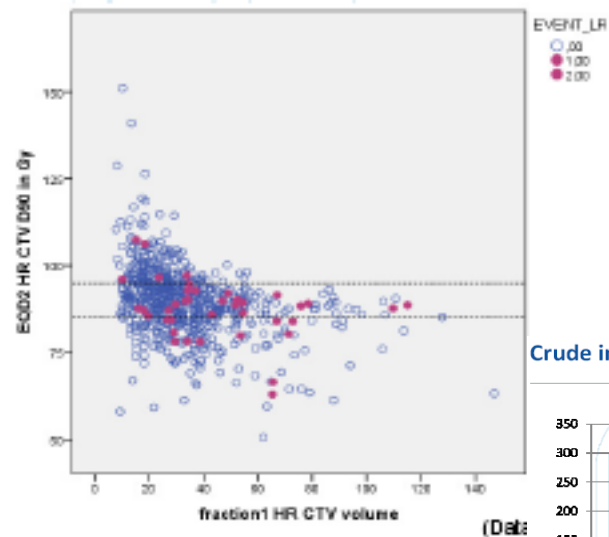
## Local Recurrences - overall



N = 714

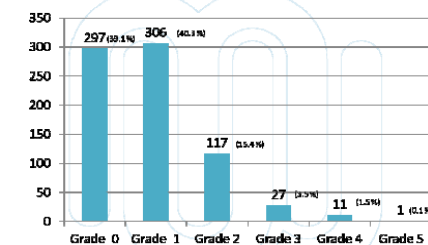
43 events

(15 incomplete remissions + 28 local recurrences)



3yr Local control:  
I: 95%, II: 90%, III: 89%, IV: 74%

Crude incidence of any GI morbidity

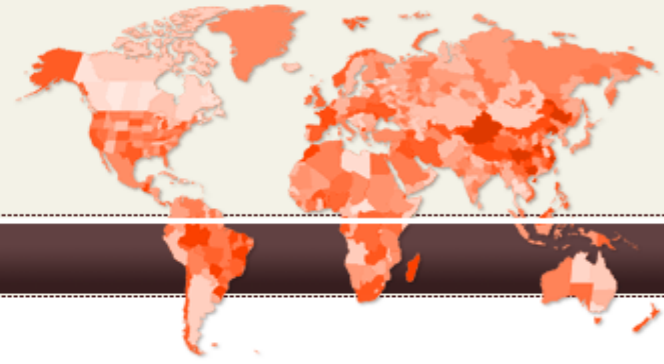


5<sup>th</sup> Annual EMBRACE Meeting – Vienna January 2014



# EMBRACE

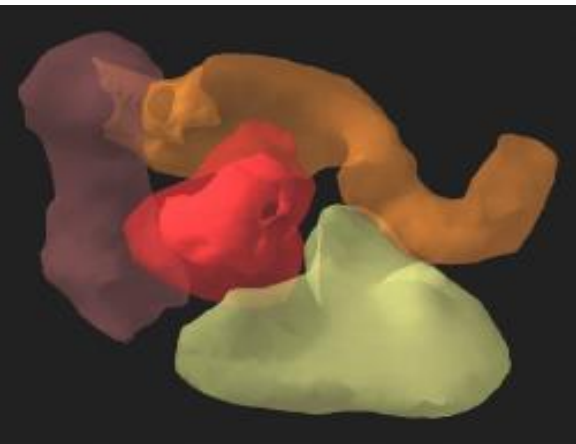
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## Events :

- **43 local recurrences**
- **76 regional recurrences**
- **98 metastases**
- **86 deaths**



# ICRU 88

## Prescribing, Recording, and Reporting Brachytherapy (BT) for Cancer of the Cervix

### Table of Contents

**Chapter (1) – Introduction**

**Chapter (2) – Prevention, Diagnosis, Prognosis, Treatment and Outcome**

**Chapter (3) – BT Techniques and Systems**

**Chapter (4) – BT Imaging for Treatment Planning**

**Chapter (5) – Oncological Concepts and Volumes and Implications  
for Adaptive Radiotherapy**

**Chapter (6) – Normal Tissue Morbidity related Concepts and Volumes**

**Chapter (7) – Radiobiological considerations**

**Chapter (8) – Dose and Volume parameters for prescribing, recording, and  
reporting of BT alone and combined with EBRT**

**Chapter (9) – Physics aspects of 3D volumetric dose assessment:  
applicator reconstruction, reference points, image fusion,  
and inter/intra-fraction uncertainties**

**Chapter (10) – Radiographic Dose Assessment**

**Chapter (11) – Sources and dose calculation**

**Chapter (12) – Treatment planning**

**Chapter (13) – Summary of the Recommendations**

# Curiothérapie guidée par l'image : conclusions

- Validation recommandations
- Homogénéité des pratiques
- Amélioration du contrôle local +++
- Diminution des complications
- Modification de l'évolution
- Métastases