



Techniques innovantes de radiothérapie

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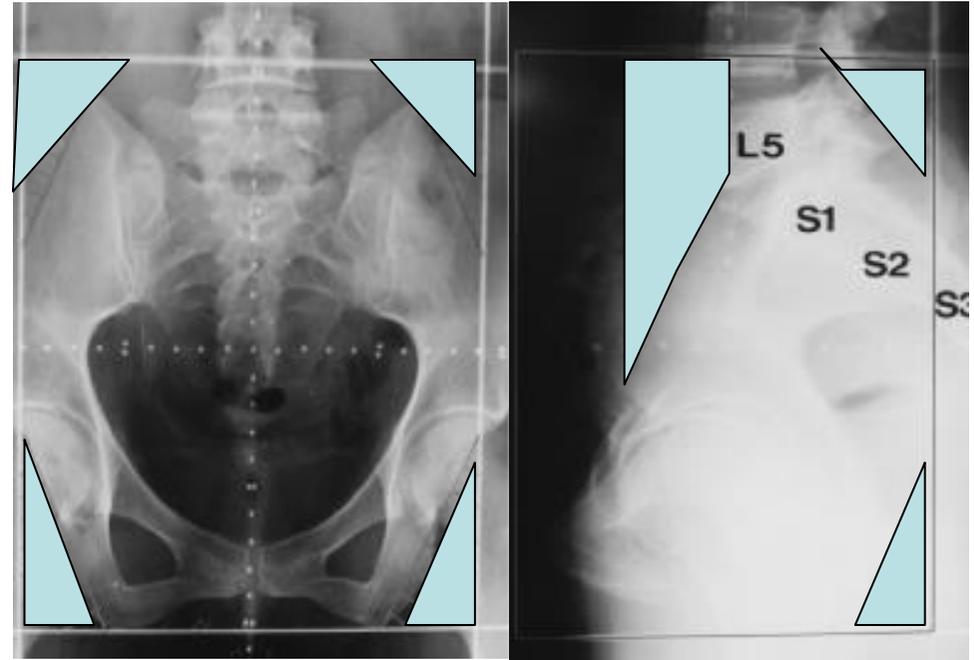
Impact de la radiothérapie conformationnelle

- Diminution significative du volume des organes critiques recevant plus de 70% de la dose prescrite :

- ↘ 34% du volume de vessie

- ↘ 15% du volume d'intestin grêle

- Meilleure couverture du volume cible



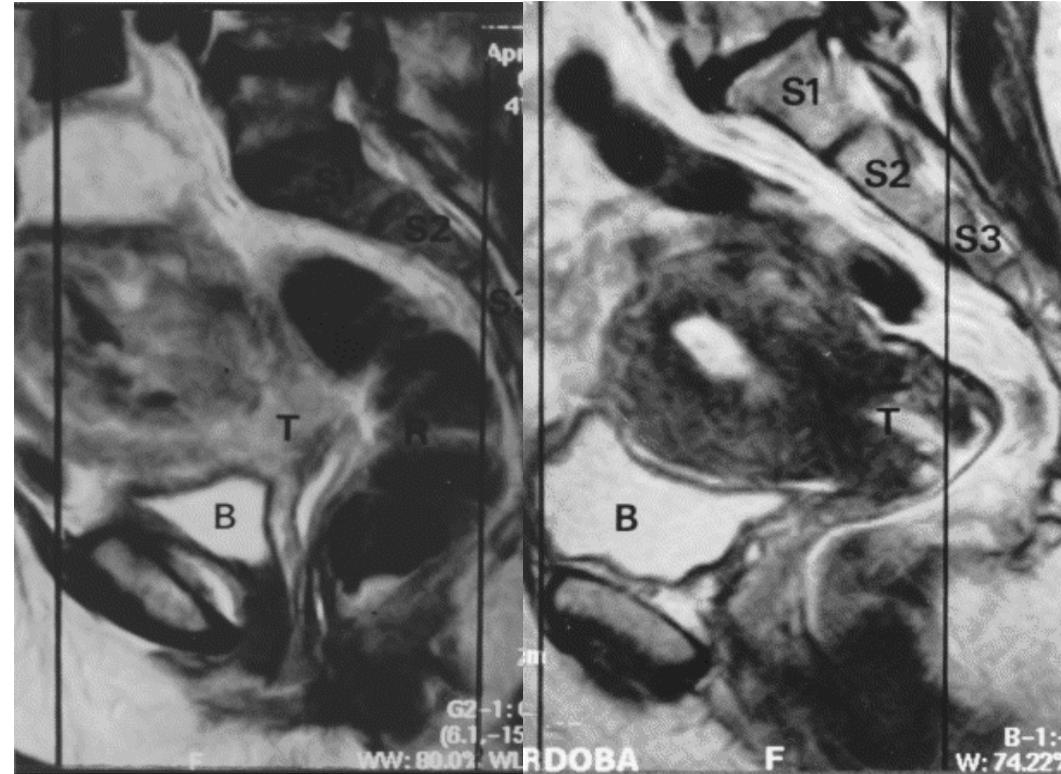
Radiothérapie 2D

Gerstner N et al . Radiother Oncol 1999;51:71-8

Impact de la radiothérapie conformationnelle

mais

- Augmentation du volume de rectum recevant plus de 70% of the prescribed dose



Gerstner N et al . Radiother Oncol 1999;51:71-8



La radiothérapie conformationnelle avec modulation d'intensité



Impact de la radiothérapie conformationnelle avec modulation d'intensité



- **Etudes dosimétriques**
- **Etudes cliniques concernant l'impact sur la toxicité**
- **Etudes cliniques concernant l'impact sur le contrôle local et la survie.**

Etudes dosimétriques (1)

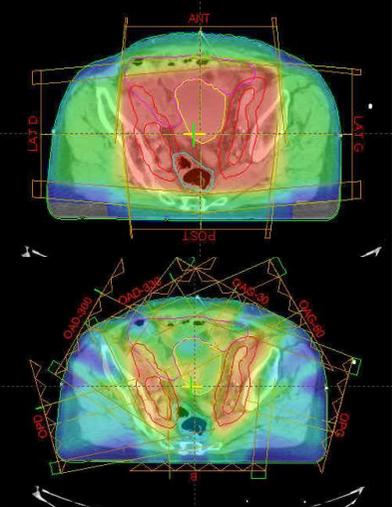


Table 2 Pooled-average volumes irradiated (%) of IMRT and 3D-CRT in different risk organs and the publication bias

Organs	Irradiated dose, Gy	No. of studies	No. of cases	Pooled volume irradiated, % (95% CI)		Egger's p-value		Begg's p-value		Studies trimmed		Adjusted volume irradiated, %		p-value*
				IMRT ⁺	3D-CRT ⁺	IMRT ⁺	3D-CRT ⁺	IMRT ⁺	3D-CRT ⁺	IMRT ⁺	3D-CRT ⁺	IMRT ⁺	3D-CRT ⁺	
Rectum	10	7	93	93.10 (83.80-97.30)	96.80 (90.00-99.00)	0.015	0.211	1.000	0.881	4	N/A	87.70	N/A	0.308
	20	7	93	87.80 (73.70-94.90)	97.50 (90.50-99.40)	0.303	0.406	0.327	0.624	N/A	N/A	N/A	N/A	0.077
	25	5	76	90.00 (79.90-95.30)	97.40 (89.30-99.40)	0.045	0.142	0.368	0.652	3	N/A	86.00	N/A	0.101
	30	7	93	68.00 (56.60-77.50)	94.40 (86.20-96.80)	0.108	0.437	0.086	0.807	N/A	N/A	N/A	N/A	0.004
	35	4	66	61.80 (48.80-73.30)	88.80 (74.70-95.50)	0.100	0.071	0.071	0.051	2	N/A	55.00	N/A	0.040
	40	7	93	48.10 (26.90-70.10)	85.40 (74.40-92.20)	0.030	0.052	0.174	0.308	N/A	3	N/A	80.10	0.002
	45	8	111	31.30 (13.20-57.70)	70.80 (59.60-80.00)	0.462	0.001	0.368	0.024	N/A	3	N/A	62.10	0.006
Small bowel	5	5	102	97.20 (90.90-99.20)	96.70 (89.50-99.00)	0.001	0.271	0.076	1.000	1	N/A	96.70	N/A	0.831
	10	8	129	88.60 (79.00-94.20)	90.00 (81.30-95.00)	0.004	0.020	0.226	0.009	4	3	82.50	86.20	0.795
	15	6	112	85.90 (74.40-92.70)	86.10 (75.00-92.80)	0.011	0.001	0.060	0.060	2	1	80.30	83.80	0.985
	20	8	129	72.30 (63.70-83.70)	78.20 (66.90-86.50)	0.637	0.001	0.711	0.009	N/A	3	N/A	71.80	0.319
	25	6	112	62.20 (44.00-77.50)	73.90 (49.10-89.30)	0.036	0.114	1.000	0.060	3	N/A	77.40	N/A	0.431
	30	8	129	43.70 (35.00-52.80)	54.80 (34.30-73.80)	0.133	0.062	0.216	0.108	N/A	N/A	N/A	N/A	0.186
	35	5	102	36.60 (27.70-46.60)	50.60 (27.50-73.40)	0.076	0.002	0.050	0.027	N/A	0	N/A	60.80	0.137
	40	8	129	24.70 (17.30-34.10)	42.50 (24.00-63.40)	0.049	0.005	0.266	0.035	3	2	28.10	58.10	0.043
	45	9	147	18.60 (12.60-26.70)	35.90 (21.90-52.80)	0.008	0.000	0.076	0.001	4	4	20.70	55.80	0.012

Yang B et al. Radiat Oncol 2012;7:197

Etudes dosimétriques (2)

Table 2 Pooled-average volumes irradiated (%) of IMRT and 3D-CRT in different risk organs and the publication bias (Continued)

Bladder	10	6	80	95.50 (86.40-98.60)	96.00 (88.40-98.70)	0.334	0.001	0.851	0.133	N/A	2	N/A	96.60	0.871
	20	6	80	88.90 (73.20-95.90)	96.00 (88.40-98.70)	0.151	0.001	0.707	0.133	N/A	2	N/A	96.60	0.169
	25	4	63	90.90 (76.60-96.80)	96.60 (87.30-99.10)	0.015		0.089	0.497	2	N/A	86.00	N/A	0.258
	30	6	80	81.20 (61.60-92.10)	94.60 (83.80-98.40)	0.227	0.153	0.133	0.260	N/A	N/A	N/A	N/A	0.079
	35	3	53	80.60 (57.70-92.70)	89.70 (70.70-96.90)	0.936	0.029	1.000	0.296	N/A	2	N/A	85.00	0.396
	40	6	80	53.60 (33.30-72.80)	76.70 (59.10-88.30)	0.260	0.176	0.133	0.133	N/A	N/A	N/A	N/A	0.090
	45	7	98	50.10 (31.70-68.50)	79.30 (54.10-92.60)	0.059	0.005	0.071	0.133	N/A	2	N/A	64.70	0.062
Bone marrow	5	5	91/143	95.20 (86.10-98.40)	97.90 (83.60-99.80)	0.833	0.112	1.000	0.807	N/A	N/A	N/A	N/A	0.501
	10	6	101/153	87.30 (73.20-93.60)	95.50 (86.00-98.60)	0.138	0.276	0.230	0.133	N/A	N/A	N/A	N/A	0.129
	15	5	94/146	74.10 (61.10-83.90)	90.80 (80.60-95.90)	0.005	0.039	0.624	0.086	3	1	68.30	90.50	0.191
	20	6	101/153	67.40 (47.50-82.50)	68.50 (55.40-79.30)	0.165	0.005	0.368	0.707	N/A	3	N/A	63.40	0.301
	25	4	61/113	62.30 (45.20-76.80)	83.40 (66.50-92.70)	0.319	0.097	1.000	0.089	N/A	N/A	N/A	N/A	0.061
	30	5	68/120	47.10 (32.50-62.20)	59.40 (44.00-73.50)	0.170	0.004	0.060	0.027	N/A	1	N/A	61.20	0.261
	35	3	51/103	36.80 (19.90-57.80)	51.70 (32.60-70.40)	0.065	0.074	0.296	1.000	N/A	N/A	N/A	N/A	0.307
	40	5	68/120	29.70 (17.50-45.70)	40.20 (26.50-55.70)	0.859	0.187	1.000	0.462	N/A	N/A	N/A	N/A	0.327
	45	4	61/113	12.80 (5.00-28.90)	31.00 (18.00-47.90)	0.070	0.099	0.308	0.089	N/A	N/A	N/A	N/A	0.068

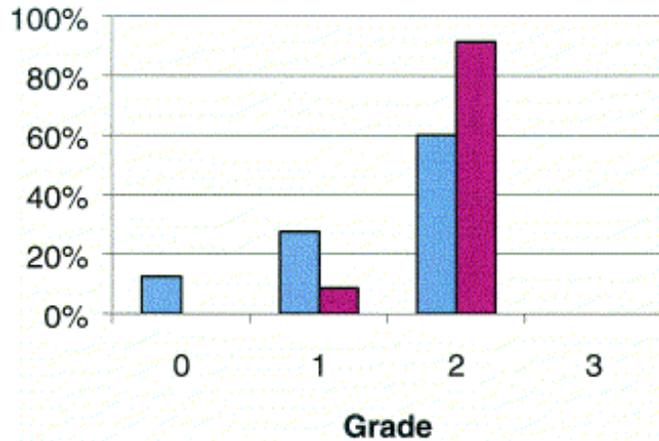
* intensity modulated radiotherapy; † three-dimensional conformal radiotherapy; ‡ p-value for comparison difference of pooled volume irradiated between IMRT and 3D-CRT.

Impact sur la toxicité (1)

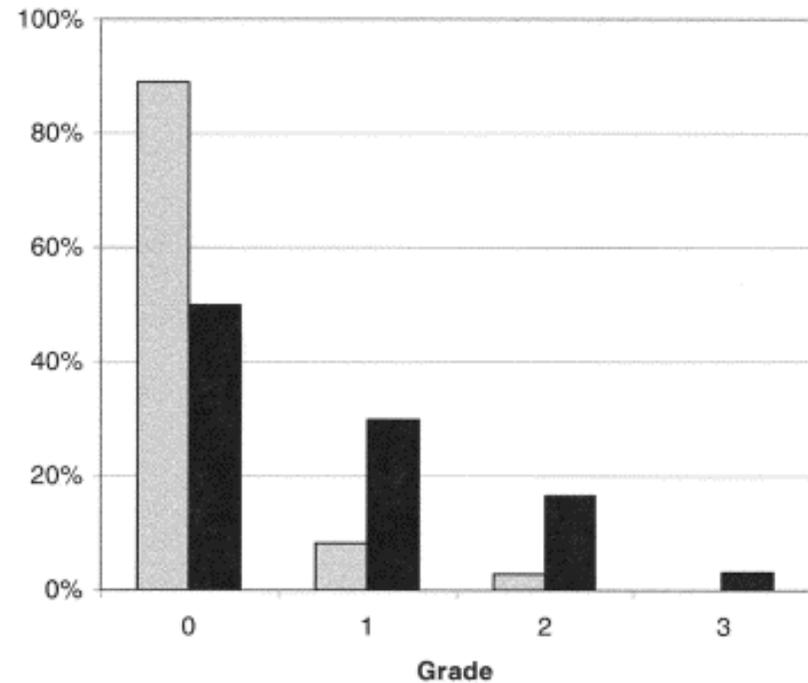
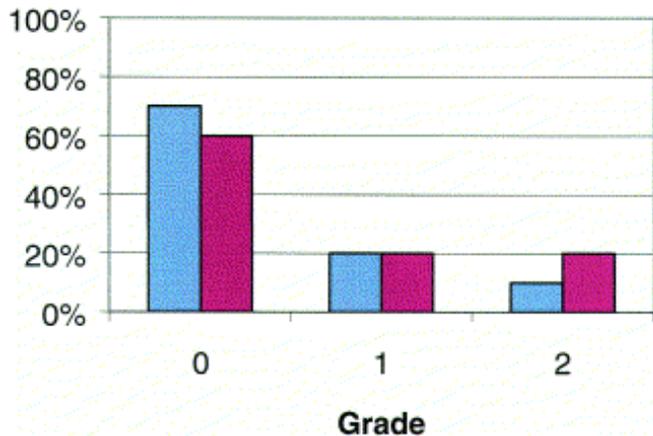
RCMI pelvienne versus Irradiation conventionnelle 4 champs en boîte



Toxicité aiguë Gastro-intestinale



Toxicité aiguë Urinaire



Complications Gastro-intestinale

Mundt AJ. *Gynecol Oncol* 2001;82:456–463
Mundt AJ. *Med Dosim* 2002;27:131–136
Mundt AJ. *IJROBP* 2002;52:1330–1337

Impact sur la toxicité (2)

CLINICAL OUTCOMES OF INTENSITY-MODULATED PELVIC RADIATION THERAPY FOR CARCINOMA OF THE CERVIX

Table 2. Toxicity

	Intact cervix (<i>n</i> = 89)		Postoperative (<i>n</i> = 22)		All patients (<i>n</i> = 111)	
	Acute	Late	Acute	Late	Acute	Late
Gastrointestinal [<i>n</i> (%)]						
Grade 0	26 (29)	61 (69)	2 (9)	20 (91)	28 (25)	81 (73)
Grade 1	25 (28)	13 (15)	6 (27)	2 (9)	31 (28)	15 (14)
Grade 2	37 (42)	11 (12)	13 (59)	0 (0)	50 (45)	11 (10)
Grade 3	1 (1)	1 (1)	1 (5)	0 (0)	2 (2)	1 (1)
Grade 4	0 (0)	3 (3)	0 (0)	0 (0)	0 (0)	3 (3)
Genitourinary [<i>n</i> (%)]						
Grade 0	53 (60)	69 (78)	15 (68)	22 (100)	68 (61)	91 (82)
Grade 1	24 (27)	13 (15)	3 (14)	0 (0)	27 (24)	13 (12)
Grade 2	12 (13)	2 (2)	4 (18)	0 (0)	16 (14)	2 (2)
Grade 3	0 (0)	3 (3)	0 (0)	0 (0)	0 (0)	3 (3)
Grade 4	0 (0)	2 (2)	0 (0)	0 (0)	0 (0)	2 (2)

Hasselle MD et al : *IJROBP* 2010, 80(5):1436-45.

Impact sur le contrôle local et la survie (1)

Table 1. Patient and tumor characteristics for the IMRT, non-IMRT, and total groups

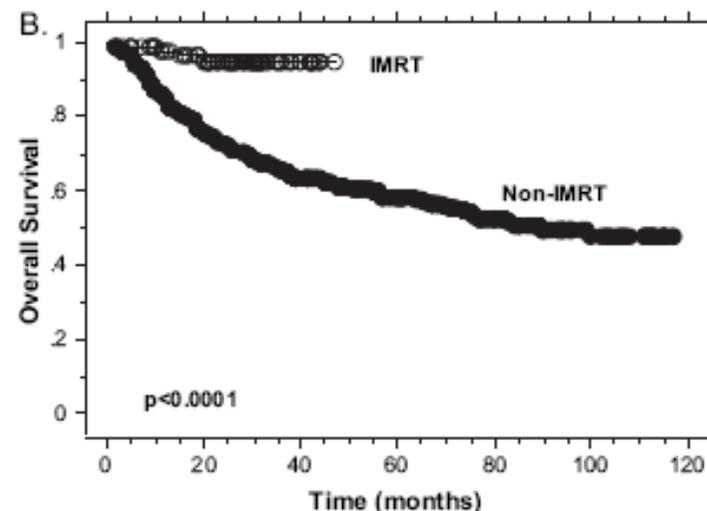
Characteristic	IMRT	Non-IMRT	Total	<i>p</i> Value
Mean age at diagnosis (y)	52	52	52	
Chemotherapy	120 (89%)	262 (83%)	449	0.2238
Stage				0.7003
Ia2	0 (0%)	2 (0.7%)	2	
Ib1	20 (14.8%)	33 (10.4%)	53	
Ib2	21 (15.6%)	56 (17.7%)	77	
IIa	3 (2.2%)	7 (2.2%)	10	
IIb	58 (43.0%)	126 (39.7%)	184	
IIIa	2 (1.5%)	2 (0.6%)	4	
IIIb	29 (21.5%)	82 (25.9%)	111	
IVa	2 (1.5%)	7 (2.2%)	9	
IVb	0 (0%)	2 (0.6%)	2	
Histology				0.3710
Adenocarcinoma	13 (9.6%)	17 (5.4%)	30	
Adenosquamous	2 (1.5%)	9 (2.8%)	11	
Squamous	117 (86.7%)	286 (90.2%)	403	
Other	3 (2.2%)	5 (1.6%)	8	
Lymph nodes				0.0309
None	68 (50.4%)	131 (41.3%)	199	
Pelvic only	41 (30.4%)	140 (44.2%)	181	
Para-aortic	23 (17.0%)	36 (11.4%)	59	
Supraclavicular	3 (2.2%)	10 (3.2%)	13	

Abbreviation: IMRT = intensity-modulated radiation therapy.

Table 2. Distribution of recurrences for the IMRT, non-IMRT, and total groups

Recurrence	IMRT	Non-IMRT	Total	<i>p</i> Value
Overall	39 (28.9%)	139 (43.8%)	178	0.036
Pelvic	11 (8.1%)	33 (10.4%)	44	
Distant	21 (15.6%)	78 (24.6%)	99	
Both	7 (5.2%)	28 (8.8%)	35	

Abbreviation: IMRT = intensity-modulated radiation therapy.





Is IMRT medically necessary for gynaecological cancers? Evidence based arguments



- If acute and chronic toxicities are the main outcomes of interest, IMRT may be considered over 3DCRT for women undergoing radiotherapy for gynaecological cancer.
- If disease-related outcomes are the main outcomes of interest, there is insufficient evidence to recommend IMRT over 3DCRT for women undergoing radiotherapy for gynaecological cancers.

Intensity-Modulated Radiation Therapy for Gynecologic Cancers: Pitfalls, Hazards, and Cautions To Be Considered

Marcus E. Randall, MD, FACR,* and Geoffrey S. Ibbott, PhD, FACR, FAAPM[†]

Intensity Modulated Radiation Therapy (IMRT) is considered a major advance in radiation therapy (RT) capability. Therefore, it has been rapidly accepted and implemented in the treatment of multiple cancers in which RT plays a major role. Early reports of IMRT in gynecologic cancers have been largely favorable, particularly in terms of decreased acute morbidity. However, IMRT has not been prospectively shown to be superior to conventional 3-dimensional RT techniques when judged against criteria established in advance. Furthermore, there are many reasons to consider the possibility that outcomes might be compromised by IMRT techniques used to treat gynecologic cancers. This article reviews the potential pitfalls and hazards of IMRT techniques on patient safety and treatment efficacy. In addition, the article describes multiple technical issues with IMRT implementation, arguing for caution in IMRT use.

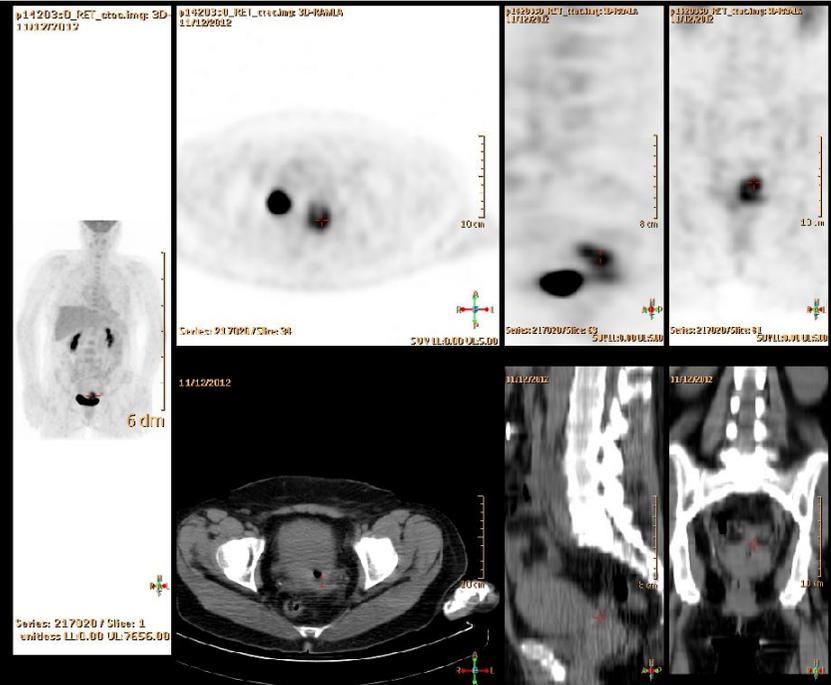
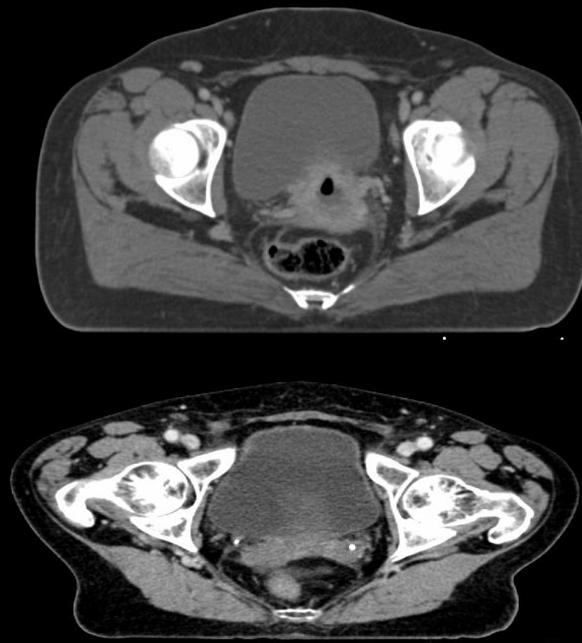
Semin Radiat Oncol 16:138-143 © 2006 Elsevier Inc. All rights reserved.

KEYWORDS Intensity Modulated Radiation Therapy (IMRT), radiation-induced malignancies, organ motion, target motion, radiobiology of IMRT



La définition et la délimitation des volumes Col utérin

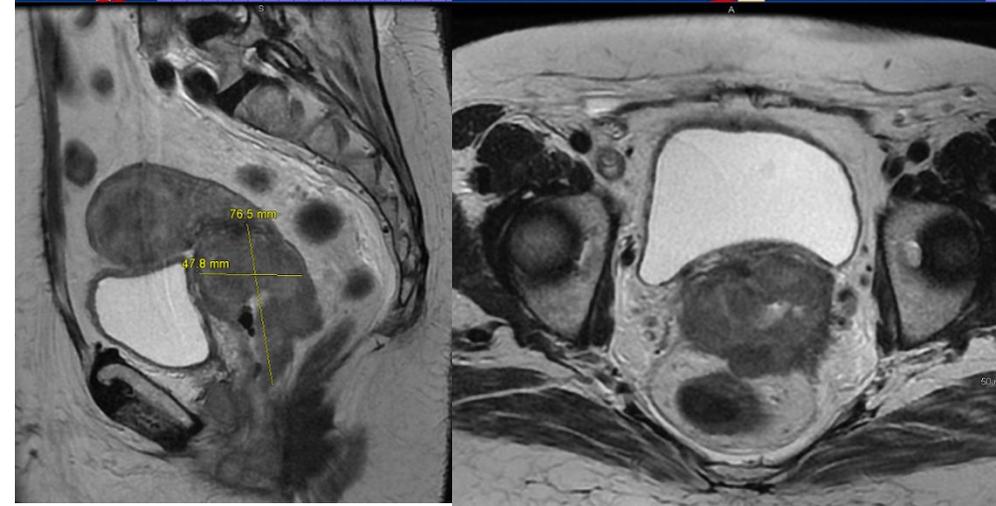
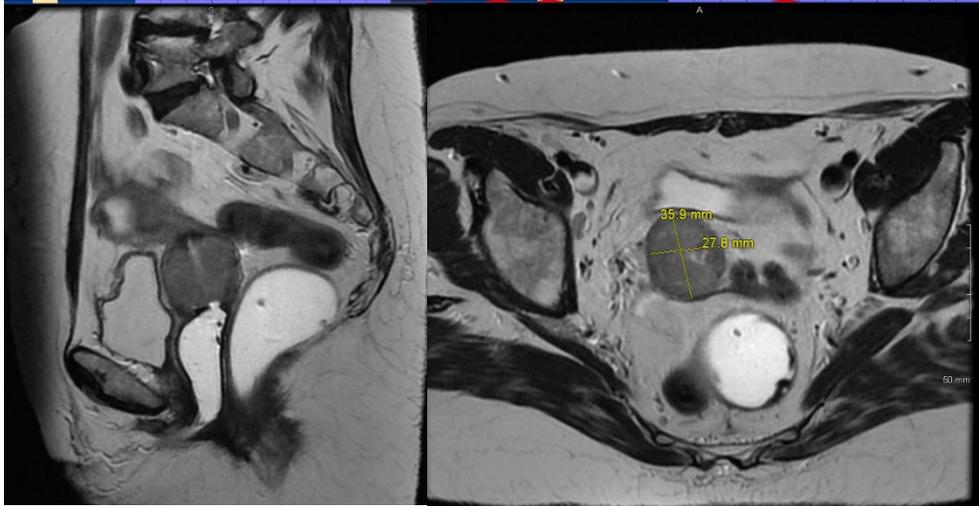
Definition du CTV



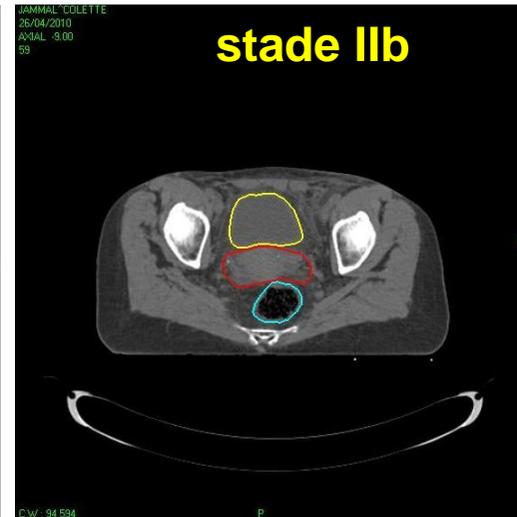
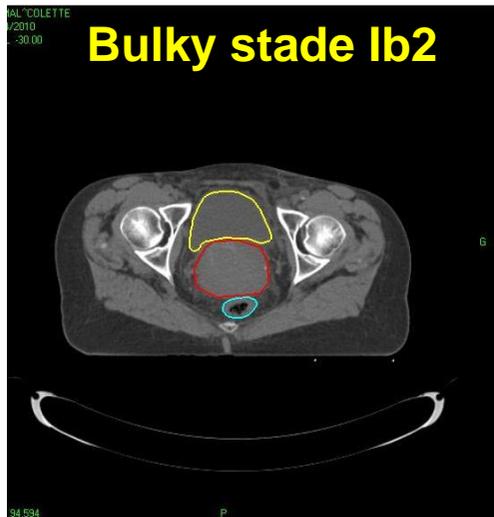
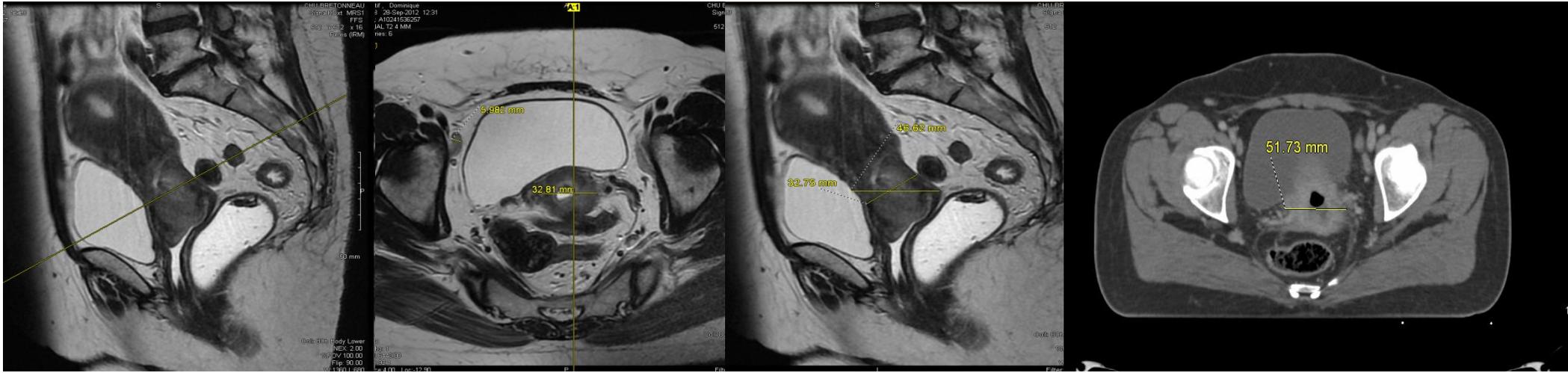
• **CTV = CTVT + CTVN**

CTVT (1)

- **CTV = la tumeur macroscopique définie par l'examen clinique et l'IRM (GTVT)**



Délinéation du GTVT



- **CTVT = GTVT**
et
Le compartiment Utérovaginal
comme produit de différenciation
du bourgeon Müllérien:
 - **Uterus + annexes**
 - **Paramètres**
 - **vagin**



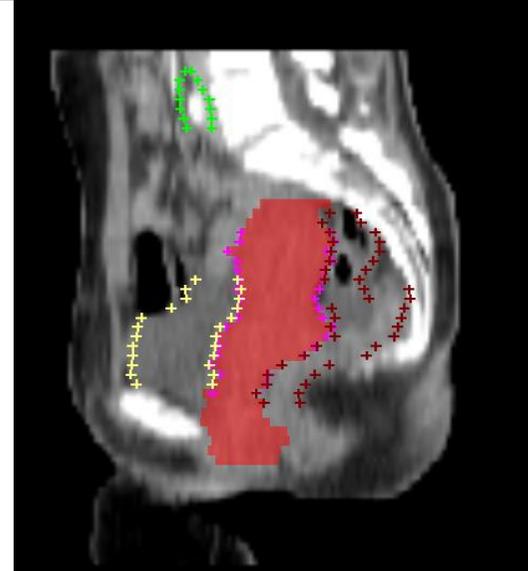
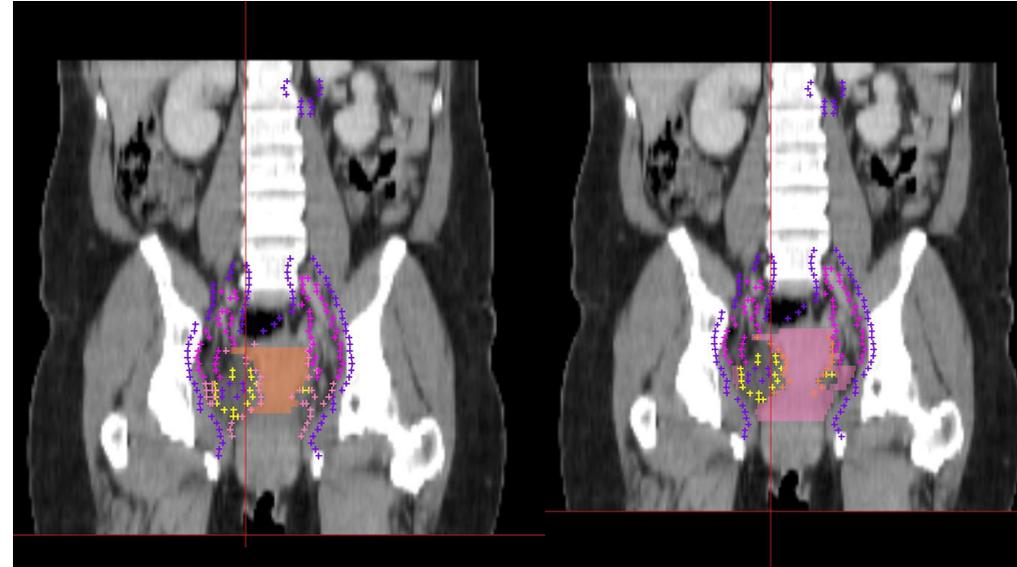
Fig. 1. Graphical representation of the uterovaginal compartment established as the differentiation product of the Müllerian anlage in the female pelvis. In this drawing the pelvic peritoneum, the right distal adnexal structures and all fatty and lymphatic tissue have been omitted to clarify the topographic anatomy. The uterovaginal compartment is highlighted in green.

CTVT :vagin

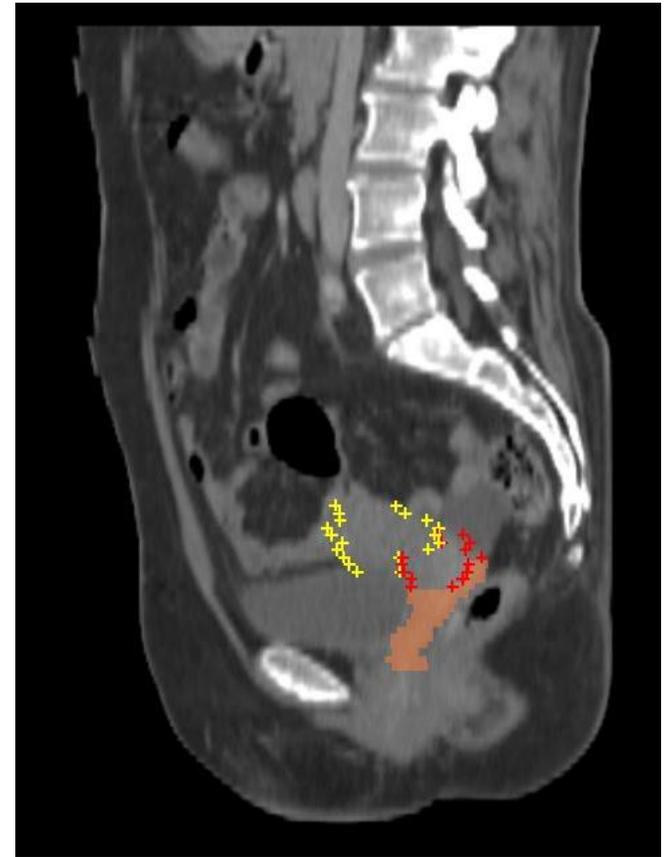
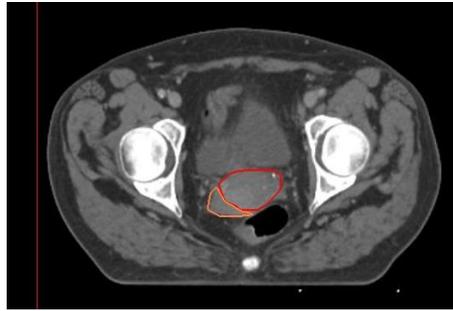
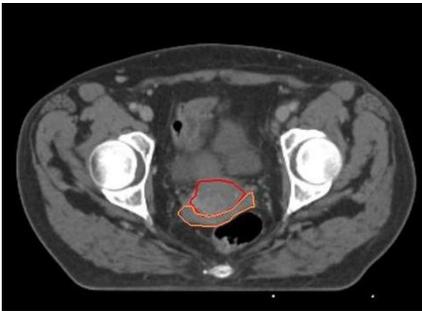
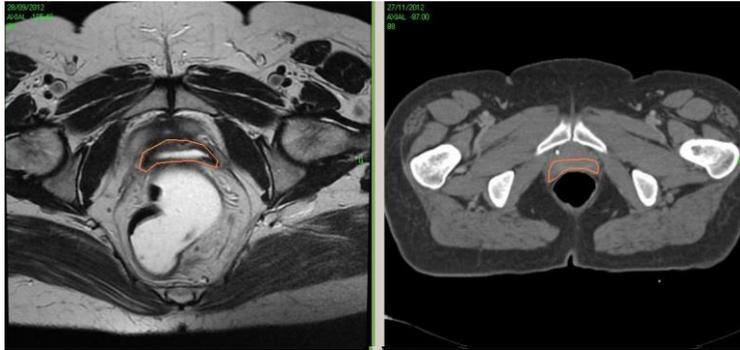
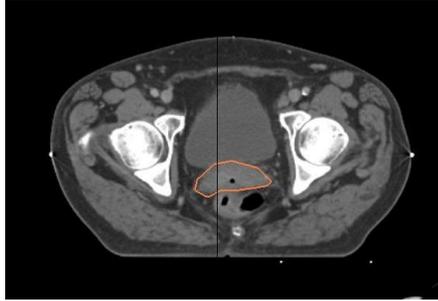
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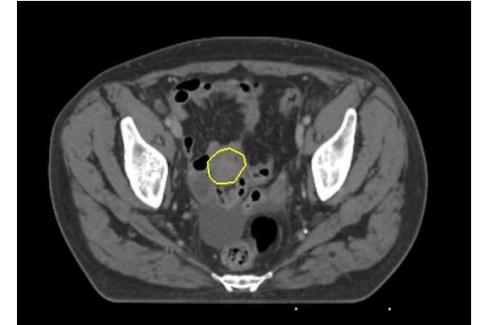
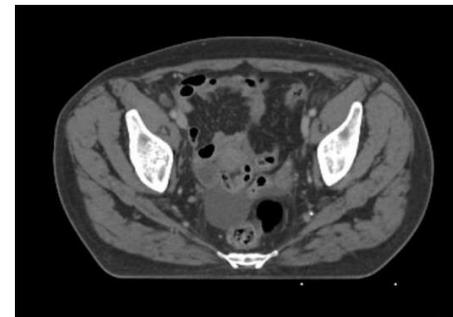
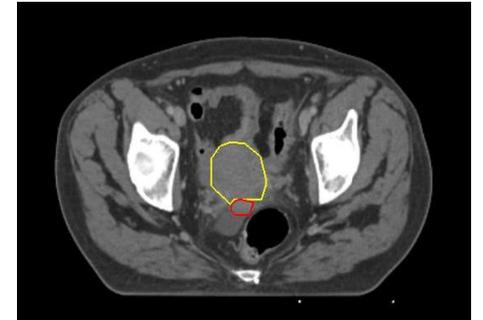
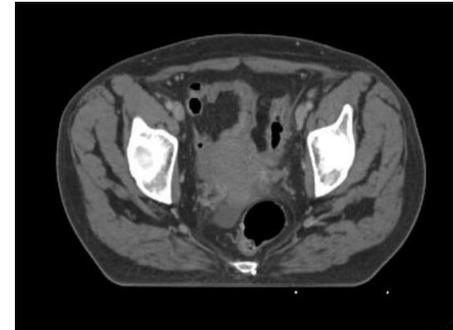
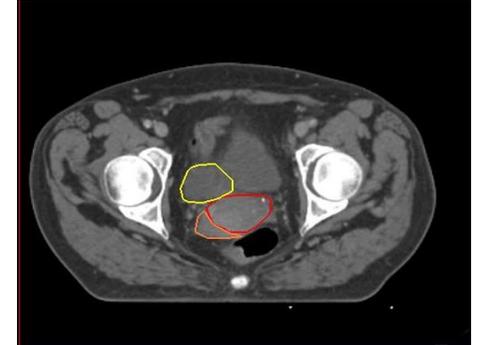
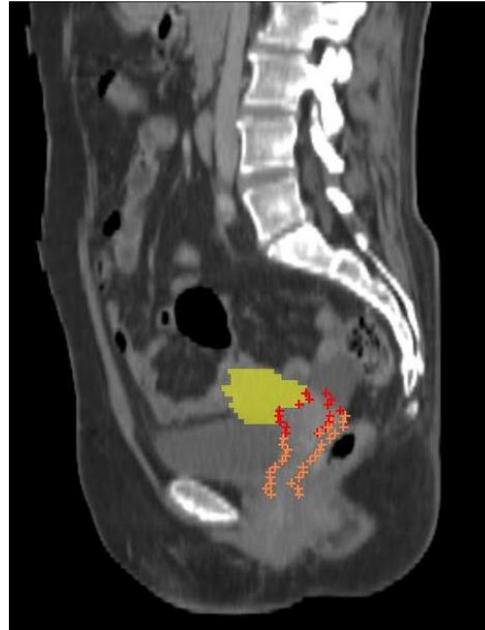
- Si pas de lésion macroscopique vaginale : 1/3 supérieur du vagin
- Si atteinte du 1/3 supérieur : 2/3 supérieur du vagin
- Si atteinte au delà du 1/3 supérieur : vagin en totalité



CTVT : Vagin



CTVT: corps utérin

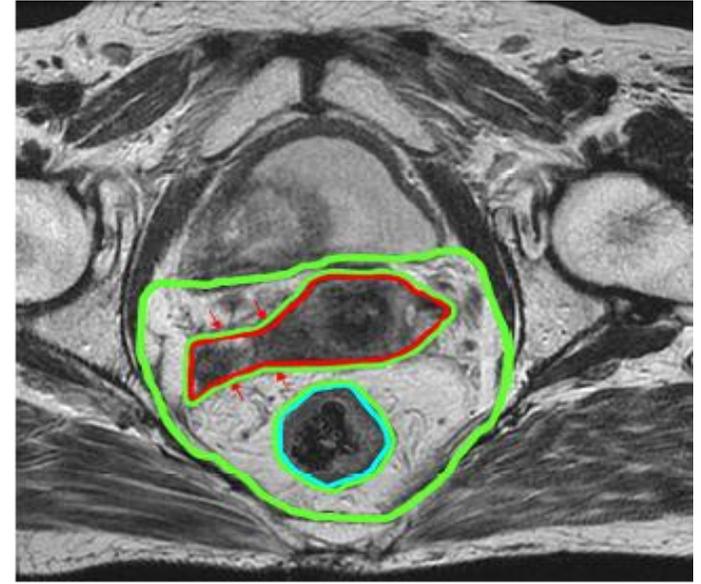
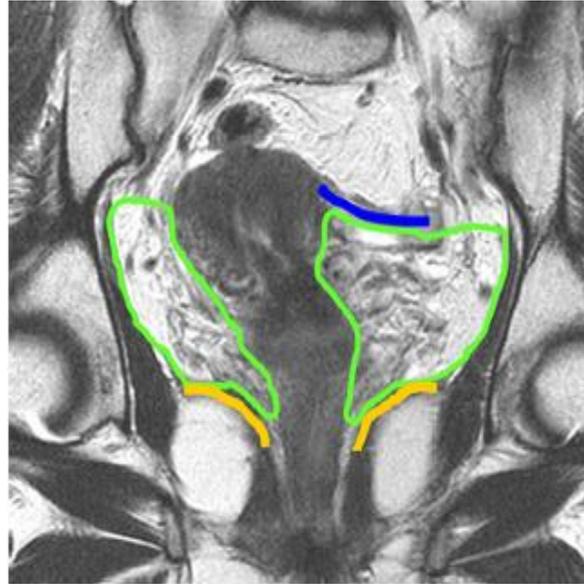
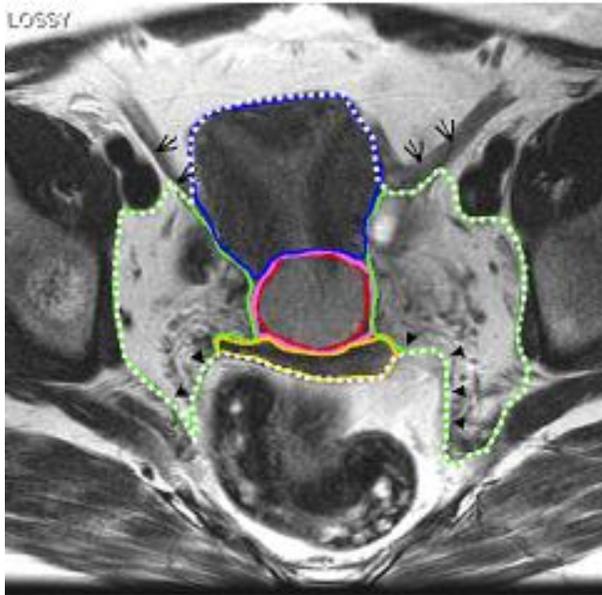


CTVT : Les annexes ?



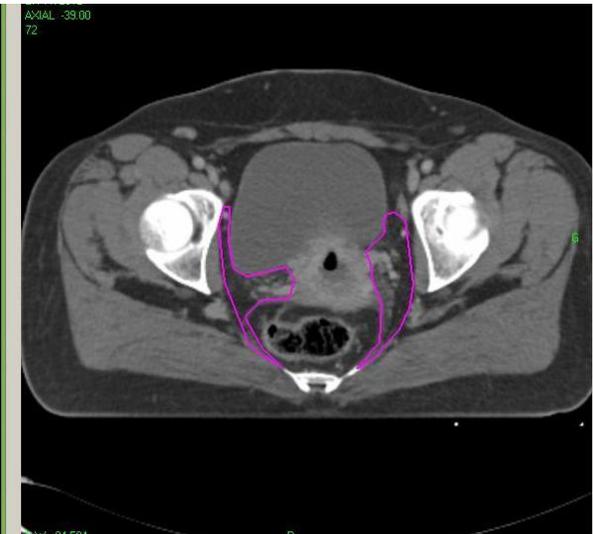
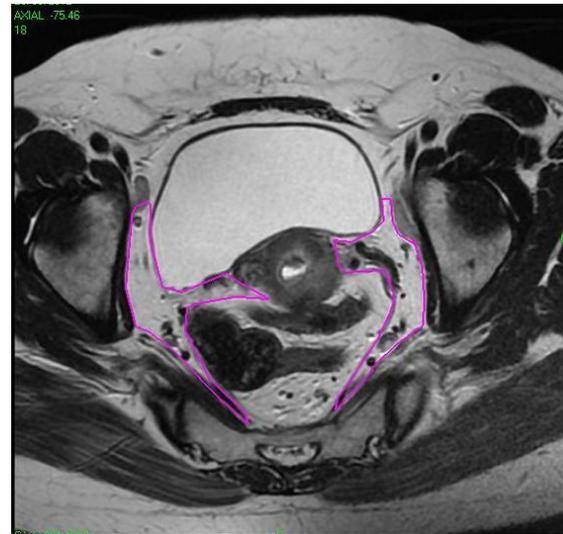
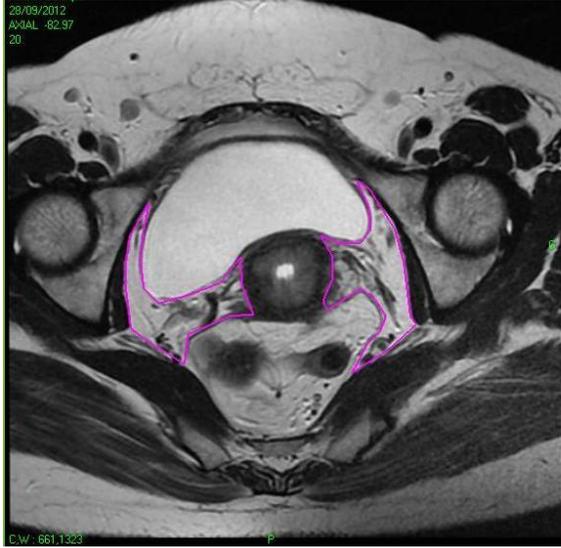


CTVT : Paramètres

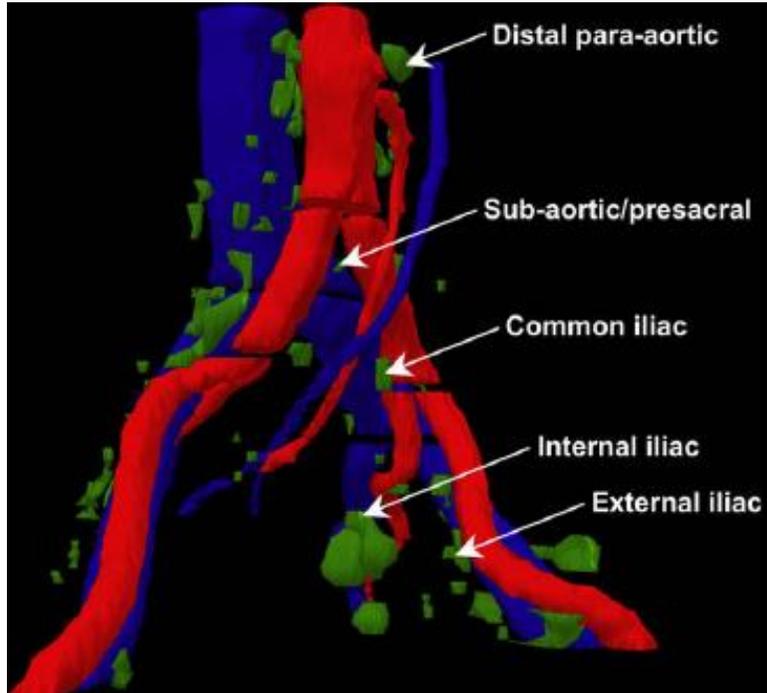


Lim K et al. IJROBP 2011;79:348-355

CTVT : Paramètres



CTVN

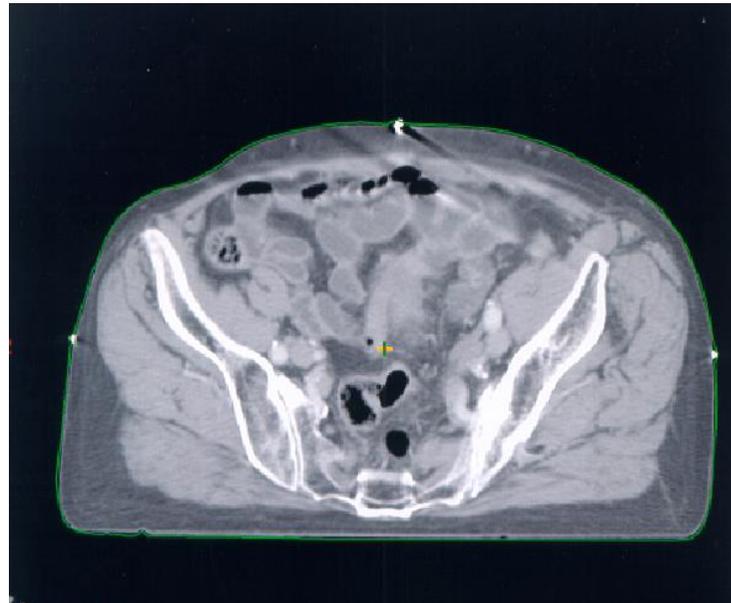


- **CTVN = Ganglions macroscopiquement envahis détectés par le(s) meilleur(s) examen(s) d'imagerie + ganglions à haut risque d'envahissement microscopique**

CTVN: quels ganglions ?

- **CTVN**

- Les ganglions ilio-obturbateurs
- Les ganglions iliaques primitifs (commun)



CTVN: ganglions lombo-aortiques

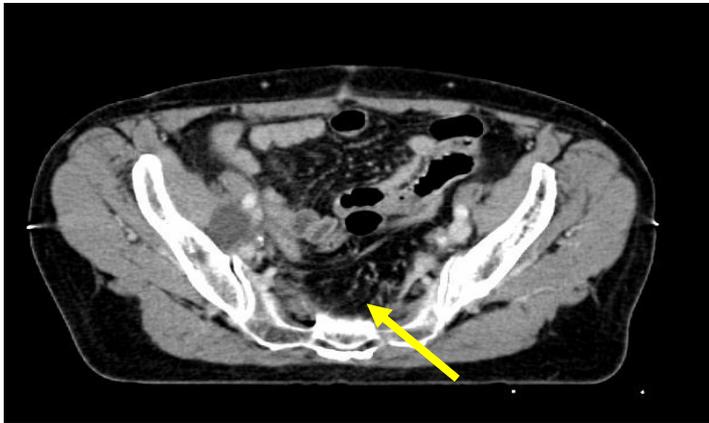


- Si envahissement lombo-aortique : **OUI**
- Irradiation prophylactique : **?**



CTVN : ganglions pré-sacrés

- Si envahissement ganglionnaire iliaque et/ou envahissement du paramètre distal ou du ligament utéro-sacré ou si la tumeur a un développement très postérieur

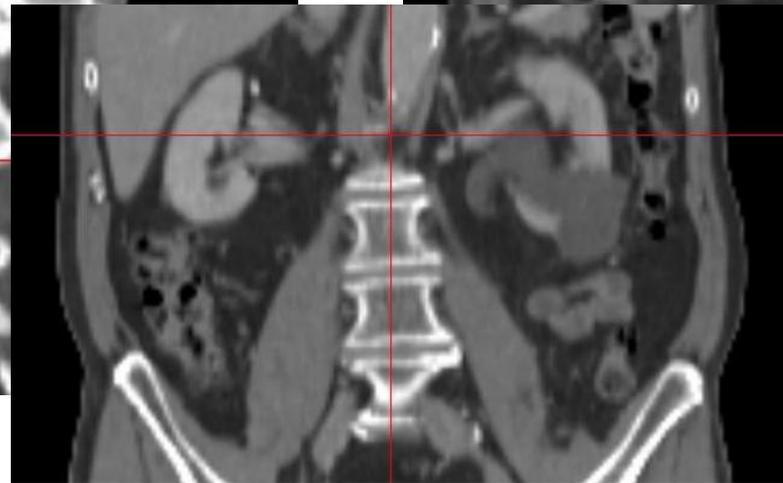
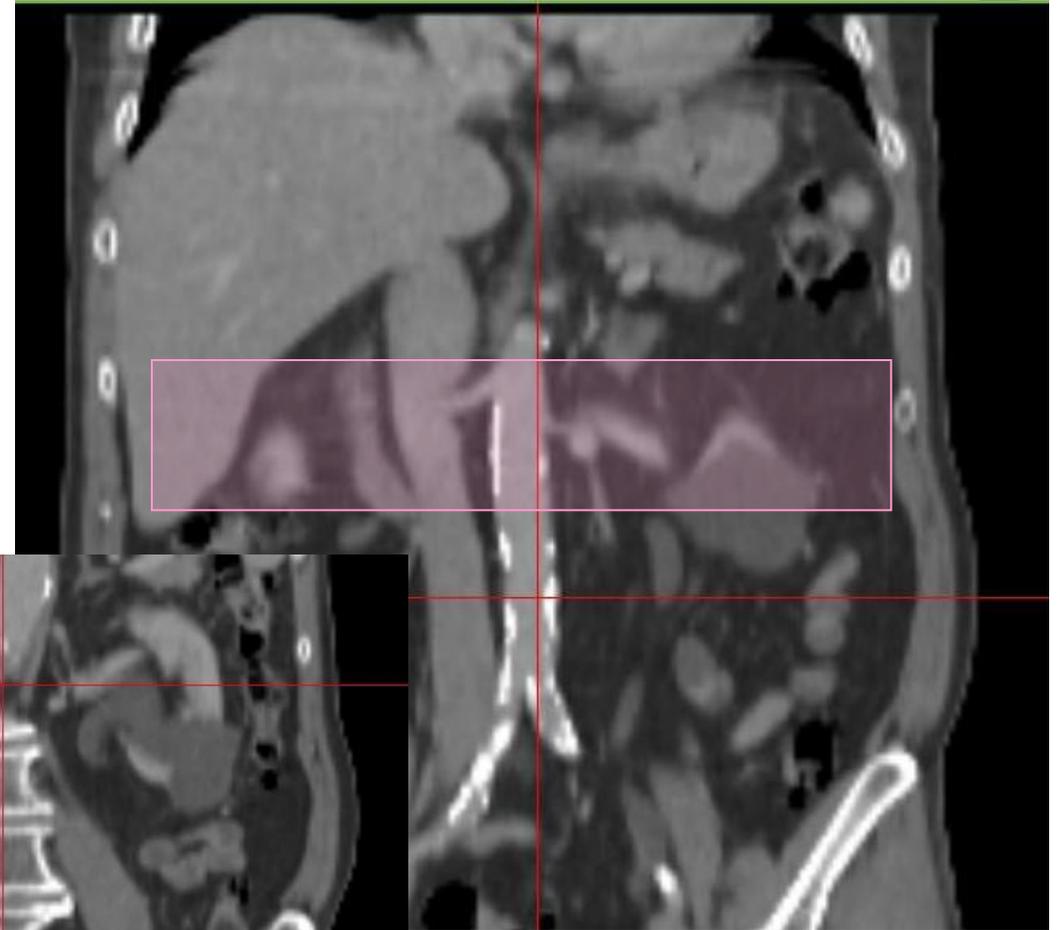
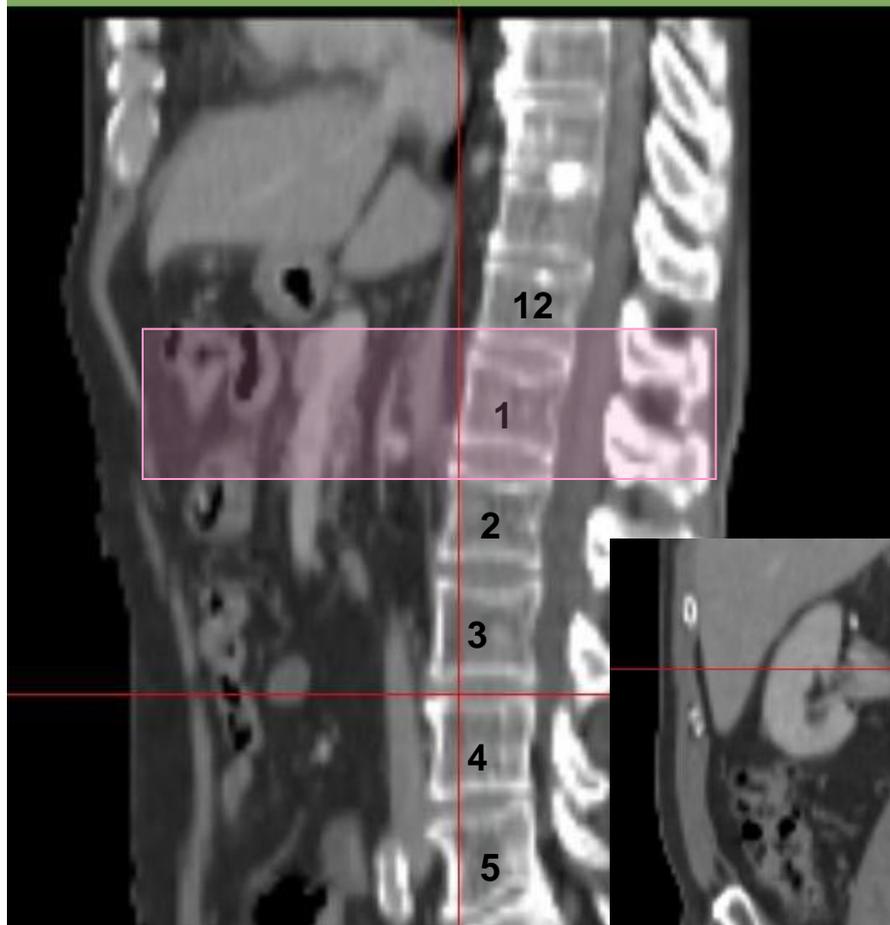


CTVN : ganglions Inguinaux

- Si envahissement macroscopique du 1/3 inférieur du vagin

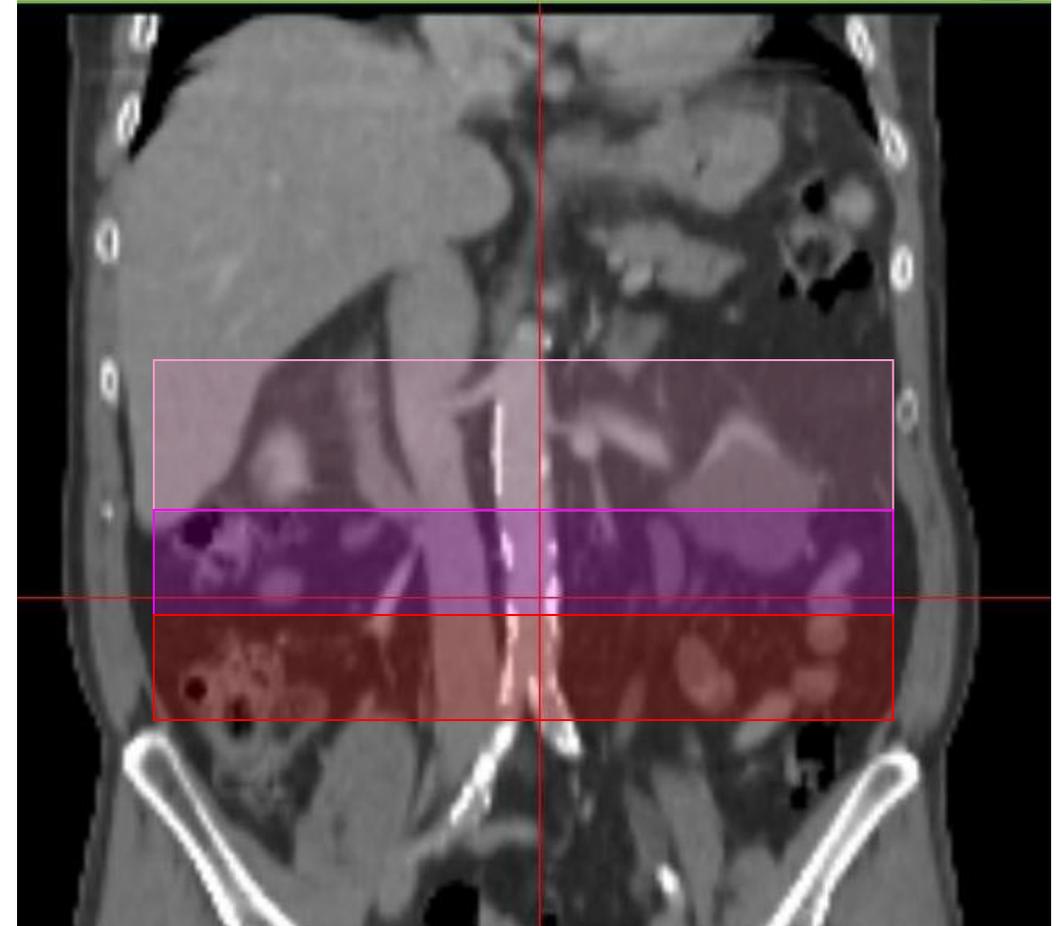
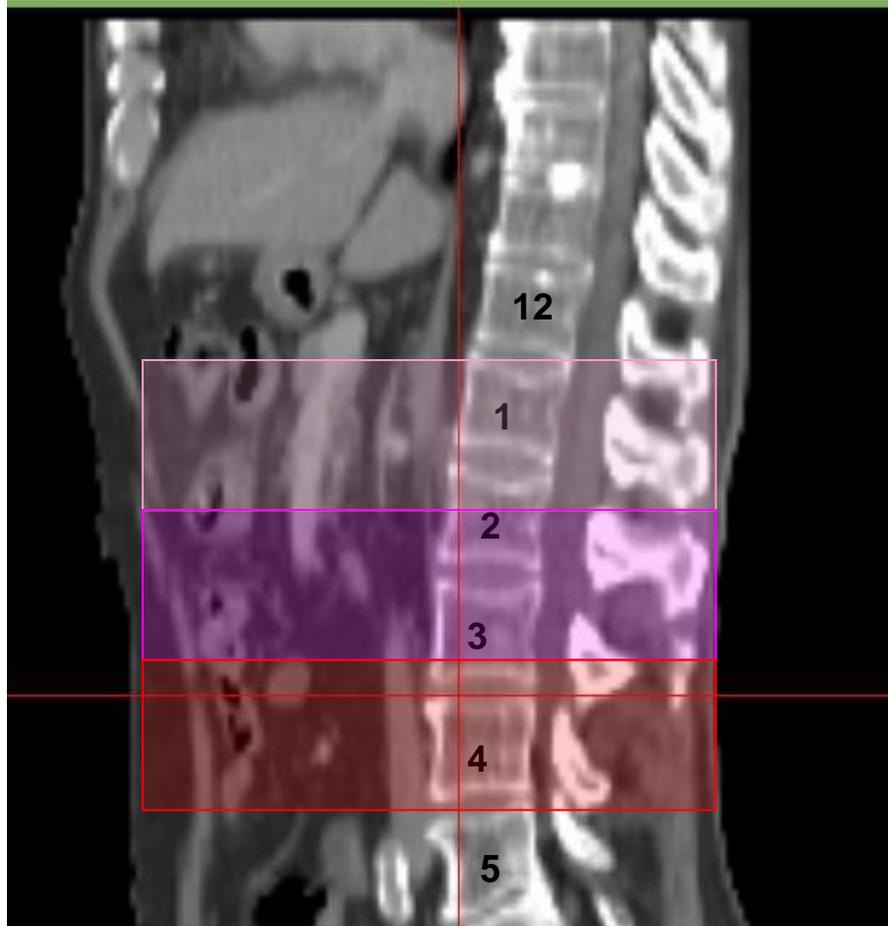


Délinéation du CTVN : Anatomie (1)



Aire lombo-aortique

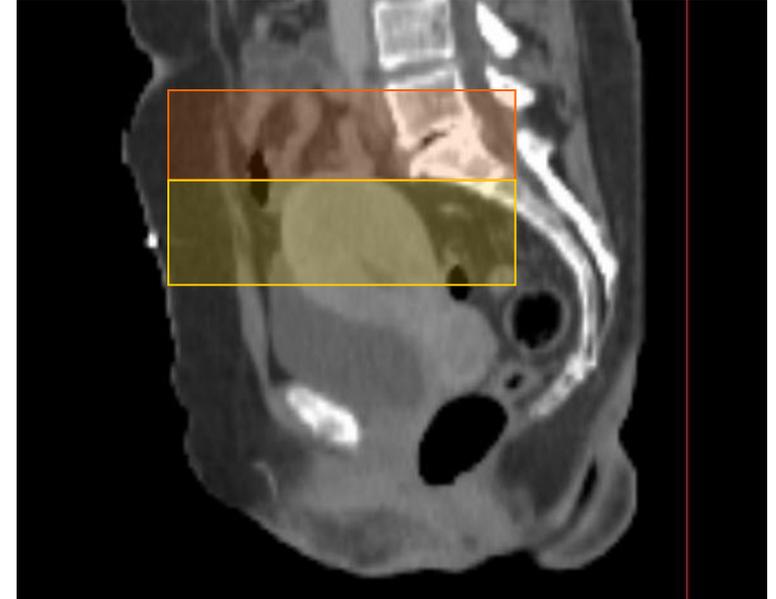
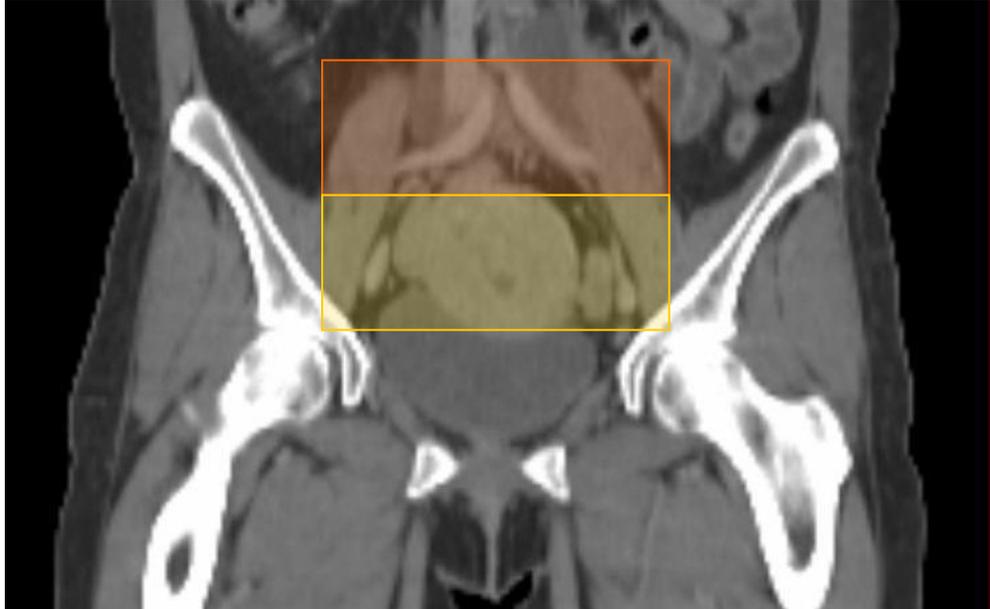
Délinéation du CTVN : Anatomie (2)



- De l'interligne (niveau de l'artère mésentérique supérieure) à la bifurcation aortique
 - Partie supérieure : de l'artère mésentérique supérieure à la veine rénale gauche
 - Partie moyenne : de la veine rénale gauche à l'artère mésentérique inférieure
 - Partie inférieure : de l'artère mésentérique inférieure à la bifurcation aortique

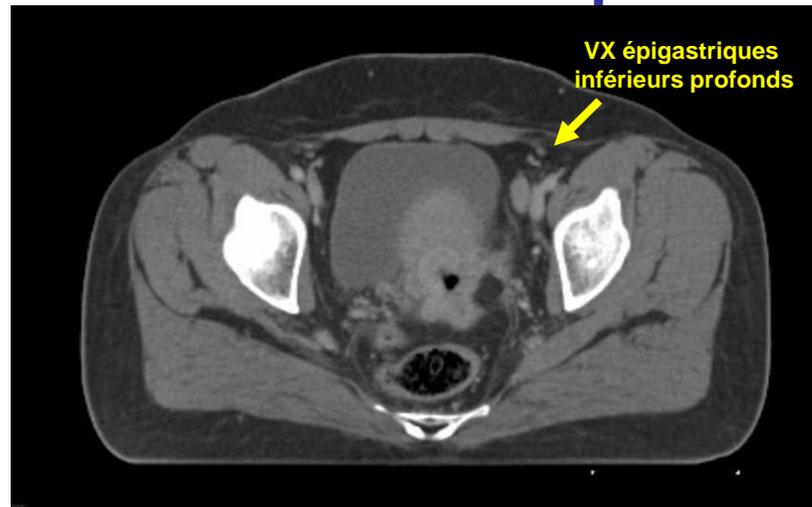
Aire lombo-aortique

Délinéation du CTVN : Anatomie (3)



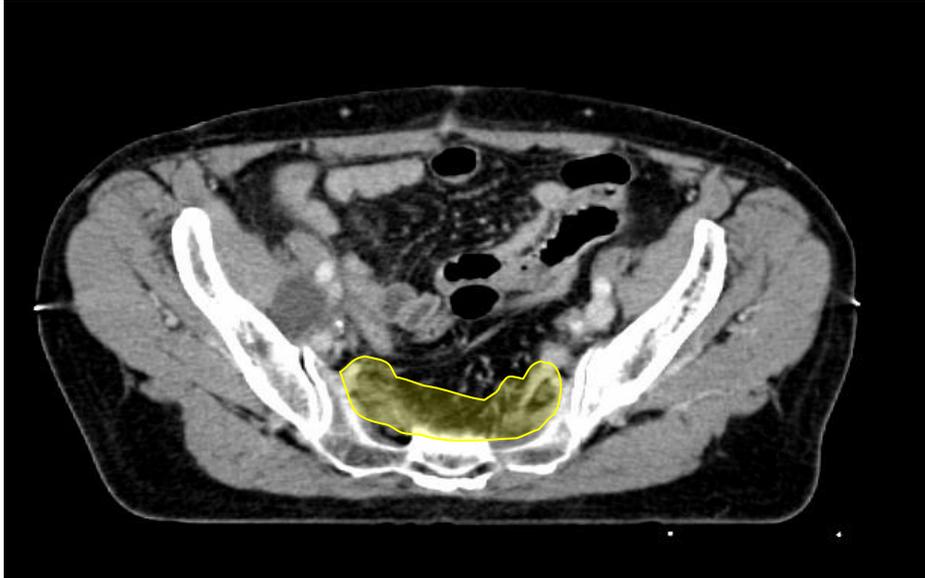
Aires iliaques

- **Iliaque primitif**
De la bifurcation aortique à la bifurcation iliaque
- **Iliaque externe**
De la bifurcation iliaque à la partie supérieure des têtes fémorales (ou au niveau des vaisseaux épigastriques inférieurs profonds)

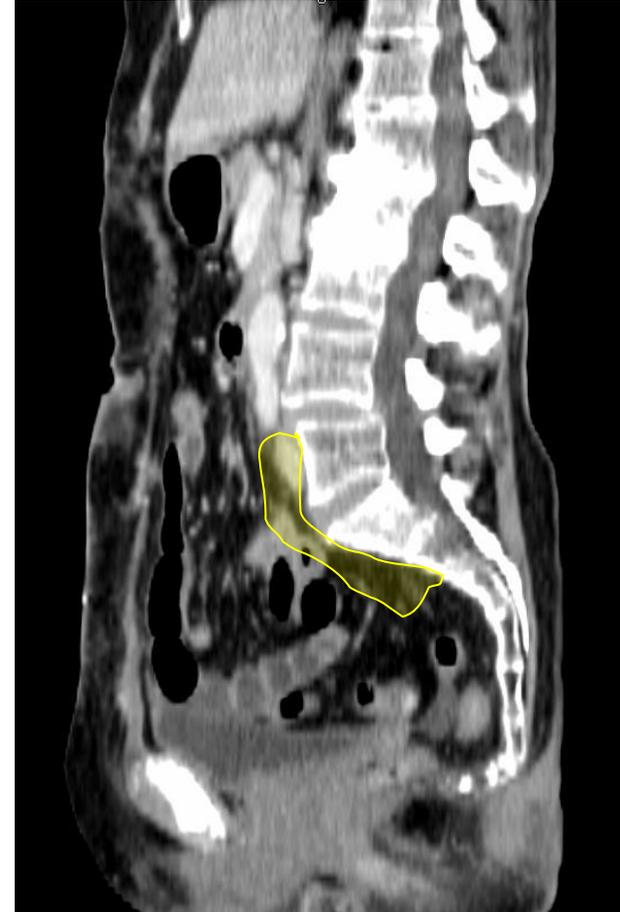


- **Iliaque interne**
De la bifurcation iliaque le long des vaisseaux hypogastriques, obturateur jusqu'au niveau des tissus para-vaginaux.

Délinéation du CTVN : Anatomie (4)



Espace pré-sacré

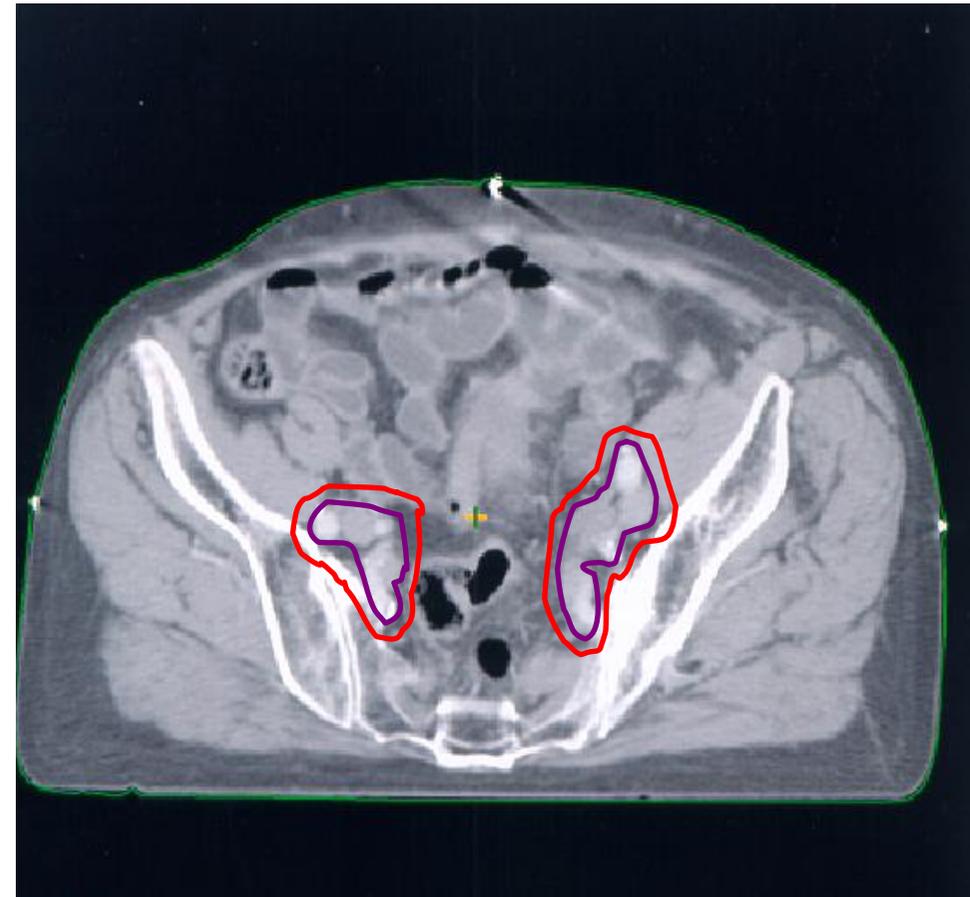


Délinéation du CTVN : Vaisseaux + 7 mm

Table 4. Recommend modifications to margins

Lymph node group	Recommended margins*
Common iliac	7-mm margin around vessels; extend posterior and lateral borders to psoas and vertebral body
External iliac	7-mm margin around vessels; extend anterior border by additional 10-mm anterolaterally along iliopsoas muscle to include lateral external iliac nodes
Obturator	Join external and internal iliac regions with 18-mm-wide strip along pelvic sidewall
Internal iliac	7-mm margin around vessels; extend lateral borders to pelvic sidewall
Presacral	10-mm strip over anterior sacrum

* Also include any visible nodes.



Délinéation du CTVN : Atlas du RTOG



External-internal iliac nodes



common iliac nodes



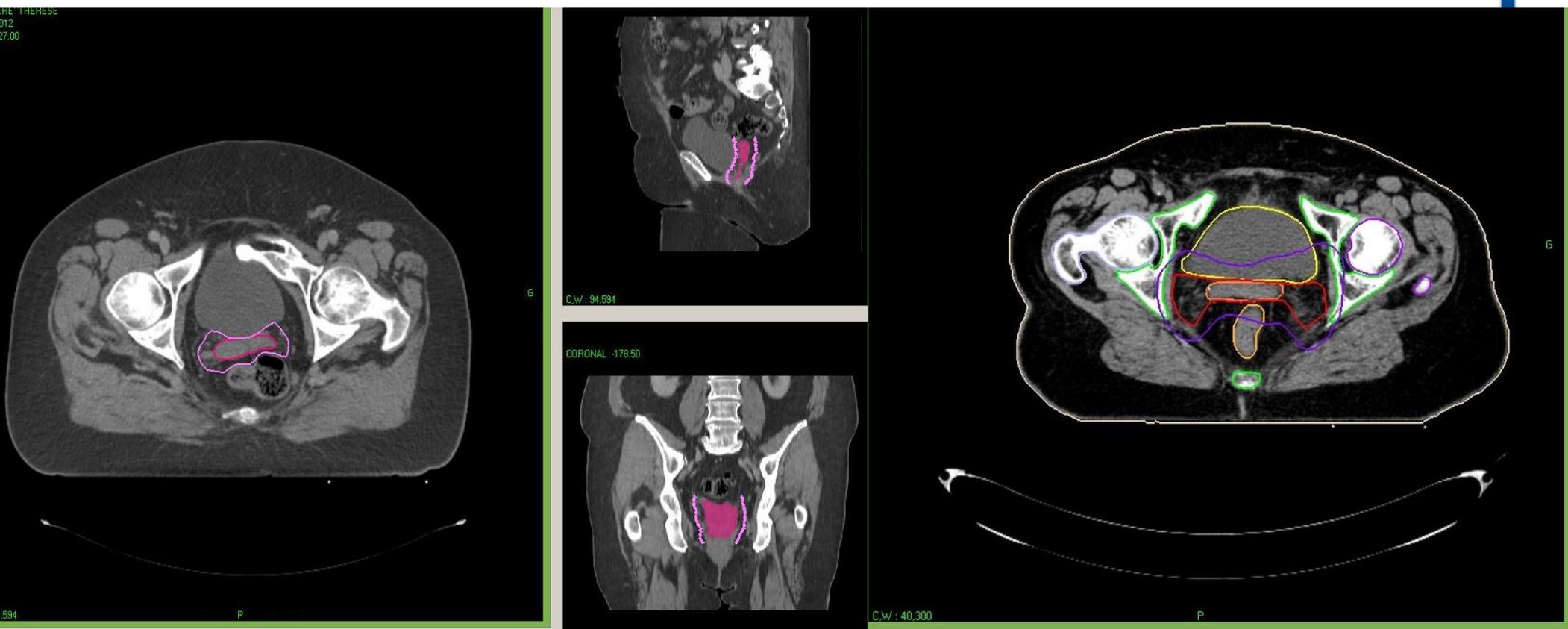
Para-aortic nodes

Small W et al. IJROBP 2008;71:428-434



La définition et la délimitation des volumes Post-opératoire

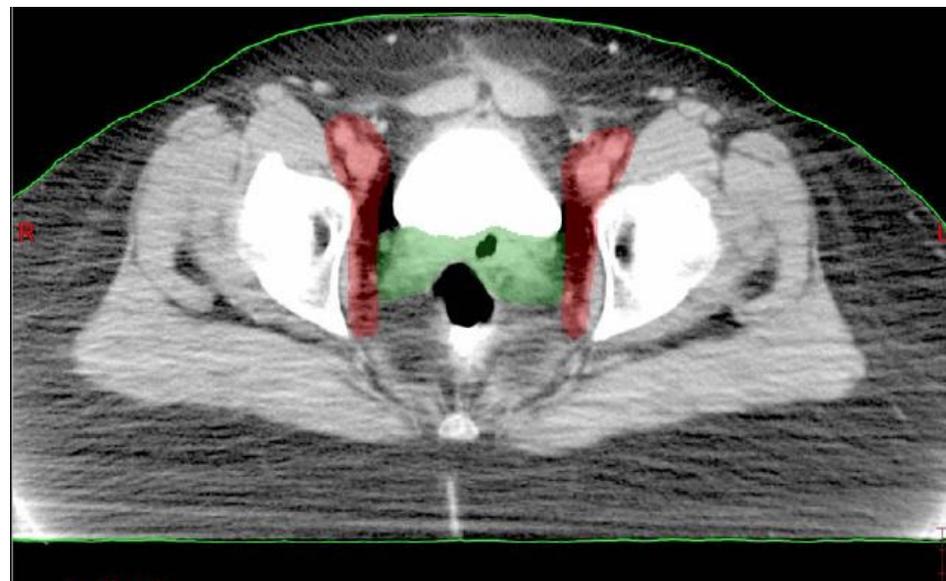
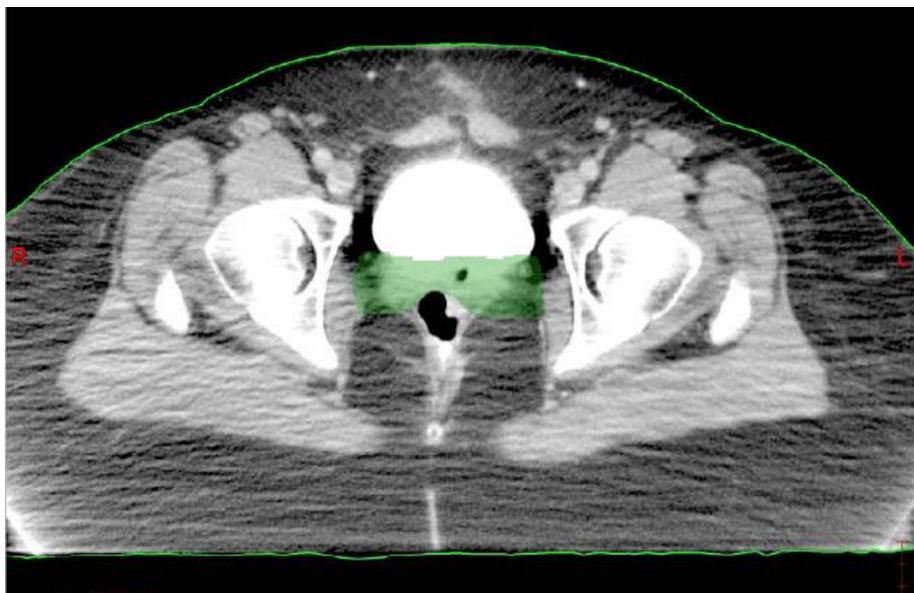
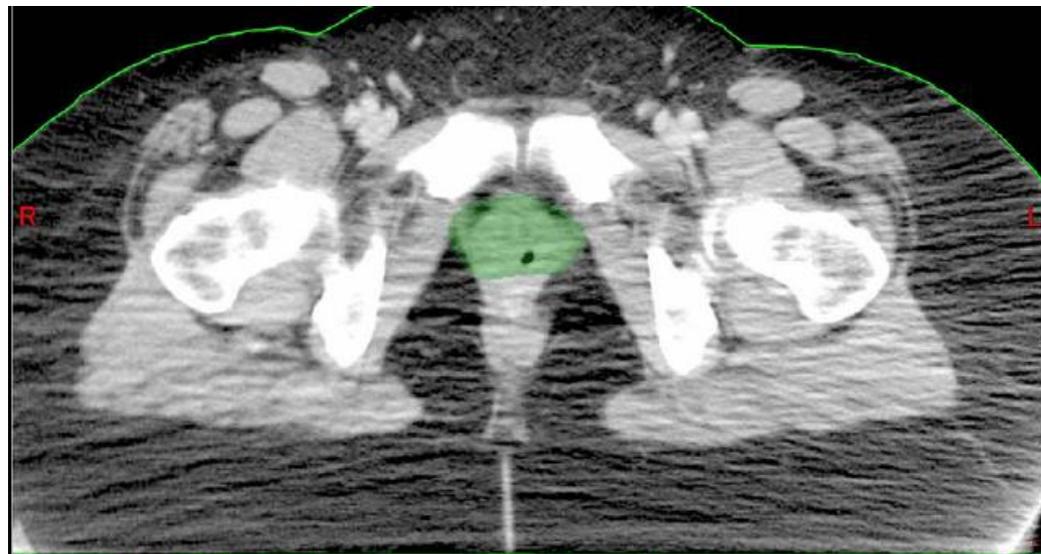
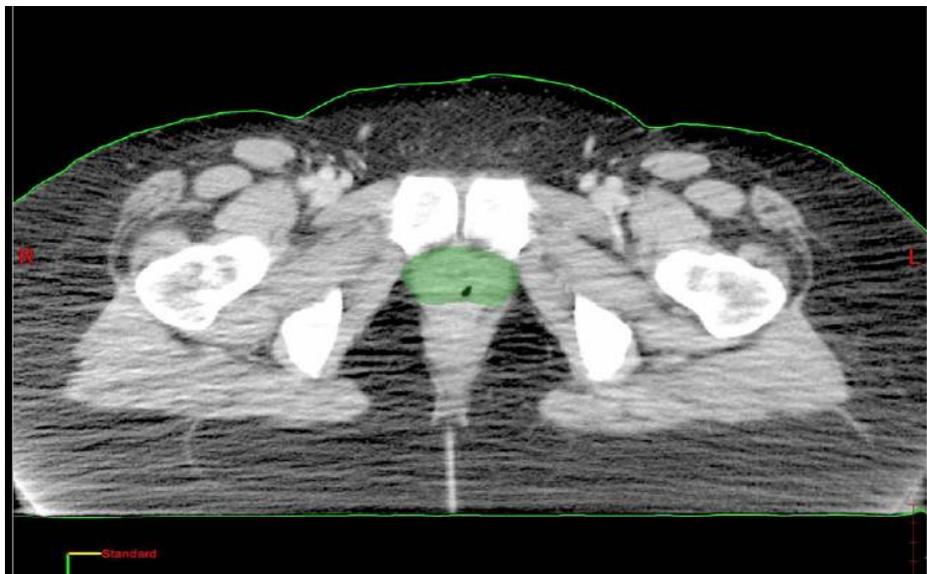
Définition du CTV post-opératoire



- Voûte vaginale et tissus perivaginaux jusqu'à la paroi pelvienne.
- Longueur de vagin en fonction du stade clinique
- 1 à 2 cm de tissus au dessus de la voûte en excluant les organes à risques.

Small W et al. IJROBP 2008;71:428-434

Atlas du RTOG

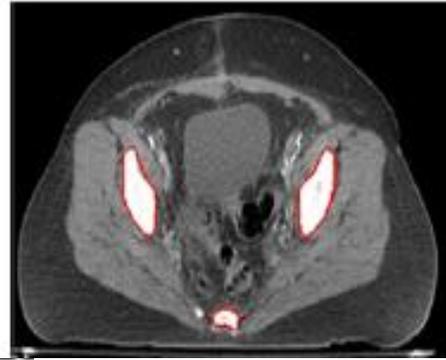


Délinéation des Organes à Risque

- **Vessie**
- **Rectum**
- **Sigmoïde**
- **Cavité péritonéale**
- **Têtes Fémorales**
- **Moelle osseuse**
- **Reins et moelle épinière si irradiation lomboaortique**

<http://www.rtog.org/CoreLab/ContouringAtlases/FemaleRTOGNormalPelvisAtlas.aspx>.

Moelle osseuse



- Moelle osseuse du bas pelvis : pubis, ischion, têtes fémorales

- Moelle osseuse des ailes iliaques



- Moelle osseuse lombo-sacrée

Essai randomisé de l'institut médical de New Dehli

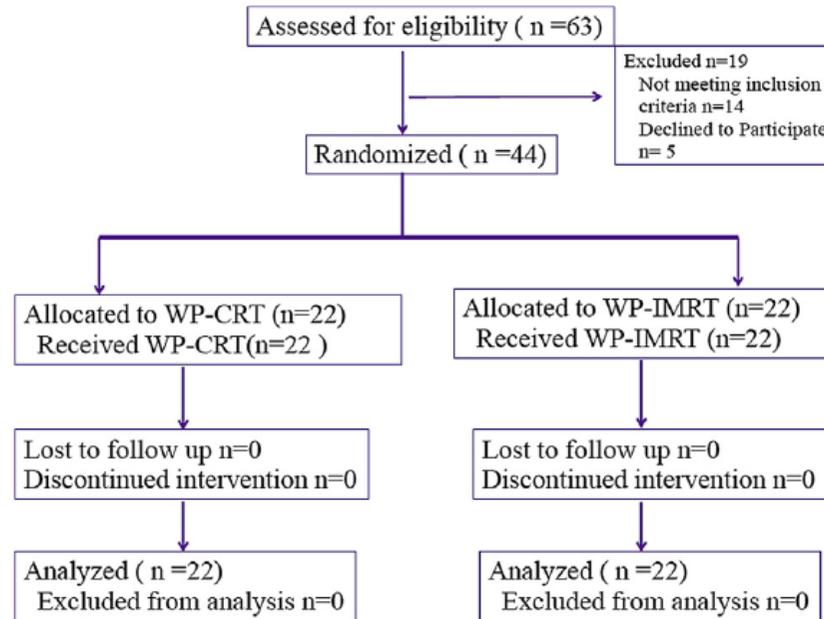


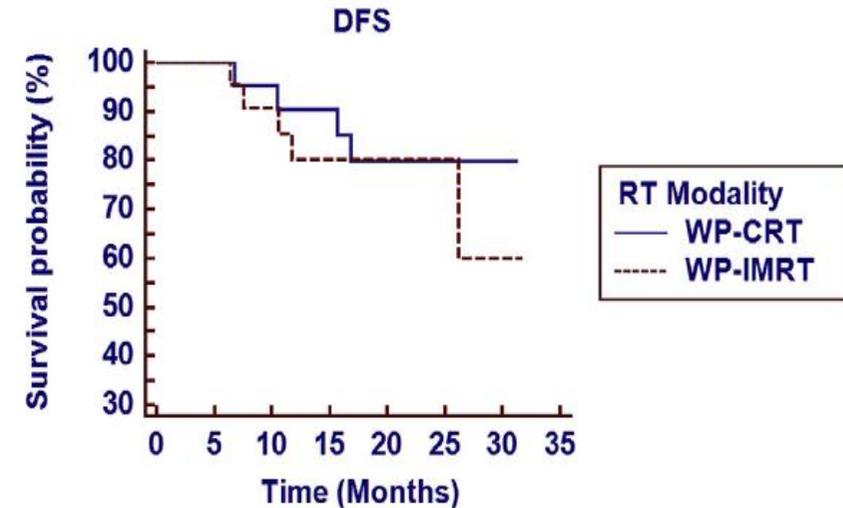
Table 3 Acute gastrointestinal and genitourinary toxicity in WP-CRT and WP-IMRT arms

Toxicity	WP-CRT arm, n (%)	WP-IMRT arm, n (%)	P value	Effect size	95% CI of the difference
Vomiting grade ≥ 2	8 (36.4)	2 (9.1)	.034	0.273	0.016 to 0.521
Vomiting grade ≥ 3	1 (4.5)	1 (4.5)	.756	0	-0.135 to 0.131
GI grade ≥ 2	14 (63.6)	7 (31.8)	.034	0.318	0.002 to 0.604
GI grade ≥ 3	6 (27.3)	1 (4.5)	.047	0.228	0.003 to 0.447
GU grade ≥ 2	7 (31.8)	5 (23.8)	.404	0.08	-0.202 to 0.361
GU grade ≥ 3	3 (13.6)	0 (0)	.125	0.136	-0.019 to 0.291

Abbreviations: GI = gastrointestinal; GU = genitourinary; WP-CRT = conventional whole pelvic radiation therapy; WP-IMRT = whole pelvic intensity modulated radiation therapy.

Essai randomisé de l'institut médical de New Dehli

- Recul médian 21,6 mois
- 3 récidives locales
 - 2 WP-CRT
 - 1 WP-IMRT
- 4 récidives à distance isolées
 - 1 WP-CRT
 - 3 WP-IMRT
- 2 récidives locales et à distance
 - 1 WP-CRT
 - 1 WP-IMRT



Number at risk

Group: WP-CRT	22	21	20	17	12	4	1	0
Group: WP-IMRT	22	22	18	11	7	5	2	0

Fig. 2. Disease-free survival of WP-CRT and WP-IMRT arm. Abbreviations: DFS = disease-free survival; RT = radiation therapy; WP-CRT = whole pelvic conventional radiation therapy; WP-IMRT = whole pelvic intensity modulated radiation therapy.

- **2 essais de phase II**

- **Essai RTOG0418**

- 43 patientes : 28% ont développé des effets secondaires aigus digestifs de grade ≥ 2

- **Essai RTCMIENDOMETRE**

- 49 patientes : 27% ont développé des effets secondaires aigus digestifs de grade ≥ 2

Jhingran A et al. Int J Radiat Oncol Biol Phys 2012; 84:e23-e28.

Klopp AH et al. Int J Radiat Oncol Biol Phys ; 86:83-90.

Barillot I et al. Radiother Oncol 2014; 111:138-143.

RCMI post-opératoire

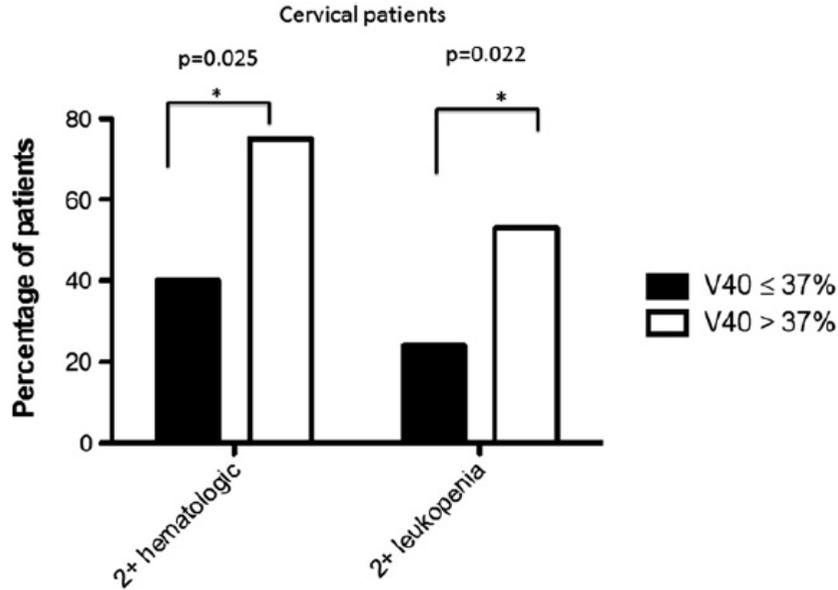


Fig. 3. Rates of hematologic toxicity and leukopenia in patients with cervical cancer with V40 greater than or less than the median value (37%). $P < .05$ by χ^2 test.

- La réduction de la toxicité hématologique est un enjeu dans le cadre des traitements par radio-chimiothérapie concomitante, et dans la perspective d'une prescription de chimiothérapie adjuvante pour améliorer la survie
- Les résultats de l'essai RCMI post-opératoire RTOG0418 démontrent que l'épargne de la moelle osseuse avec la RCMI permet de réduire la toxicité hématologique
- Le volume de moelle osseuse recevant 40 Gy ou plus est un facteur de risque significatif du développement de la toxicité hématologique



Contraintes de dose aux volumes cibles



- **Selon le rapport ICRU 50-62**
 - 100% du CTV doit recevoir la dose prescrite
 - Le PTV ne doit pas recevoir moins de 95% de la dose prescrite et pas plus de 107%
- **Mais en modulation d'intensité on peut accepter une hétérogénéité plus importante pour le PTV**
 - 95% du PTV ne doit pas recevoir moins de 90% de la dose prescrite, 5% ne doit pas recevoir plus de 115% de la dose prescrite et 1% plus de 120%
- **Comment rapporter la dose**
 - D98% (near minimum dose)
 - D50% ou Dmédiane
 - Dmoyenne
 - D2% (near maximum dose)
 - D_v v= % de volume important dans le contexte.

Contraintes de dose aux organes à risques

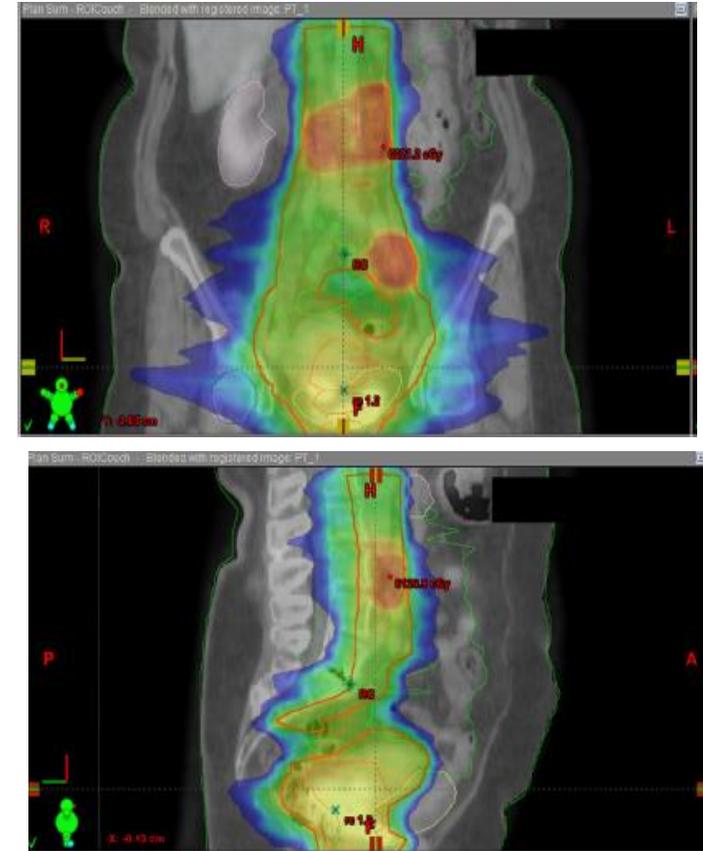
- Les contraintes habituelles vessie/rectum ne s'appliquent pas car la dose délivrée est de 50 Gy ou moins en irradiation externe.

Pelvis	
Vessie	V60 Gy < 50% ; V70 Gy < 25%
Rectum	V60 Gy < 50% V70 Gy < 25% V74 Gy < 5%
Canal anal	D max sur tout le canal 55 Gy
Têtes fémorales	V50 Gy < 10%
Os en général	D max 60 Gy

- EN RCMI
 - D2% = dose prescrite et V45Gy \leq 40% pour le rectum, sigmoïde et la vessie
 - V45Gy \leq 300-350 cc pour la cavité péritonéale
 - V40 Gy \leq 37% pour la moelle osseuse

RCMI = outil pour l'escalade de dose

- 2003-2012 : 61 patientes
 - Schéma de traitement :
 - 45 Gy/1.8 Gy/ fraction champs étendus
 - 55 Gy/2.2 Gy/ fraction SIB sur les ganglions hypermétaboliques
 - CDDP hebdomadaire
 - 179 ganglions
 - 67% pelvis , 33% pelvis + lombo-aortique
 - Taille moyenne : 1.8 cm
 - Resultats
 - Réponse Complete à 12 semaines : 77%
 - Recul Médian: 29 mois
 - 3% de tumeur résiduelle ou de récidence
 - 4% \geq grade 3 toxicité gastro-intestinale (CTCAE-4.0)



Intensity modulated radiotherapy in gynecologic cancers: Hope, hype or hyperbole?

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HIGHLIGHTS

- IMRT's use in gynecologic cancer is evolving
- The use of IMRT in postoperative gynecologic cases should be considered
- Care must be taken with the use of IMRT secondary to unique planning concerns.

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ABSTRACT

Significant advances have occurred within the field of radiation oncology within the past few decades. Treatment with external beam radiotherapy has progressed from treatment fields planned from bony anatomy seen on planar X-rays, to 3-dimensional planning utilizing fused MRI's and PET images. Recently, intensity modulated radiotherapy (IMRT) has been integrated into many areas within radiation oncology, and its role in the treatment of gynecologic cancers is evolving. Potentials exist for improvements in both treatment toxicity, as well as improved efficacy through advances in treatment delivery. Unique challenges are also raised, however. With increased accuracy of treatment delivery comes the need for greater accuracy in target delineation and incorporation of motion to prevent marginal misses. The goal of this review is to evaluate the use of IMRT in cervical and endometrial cancers, including the results of dosimetric and clinical studies to date. In addition, potential disadvantages and challenges of IMRT integration are discussed.

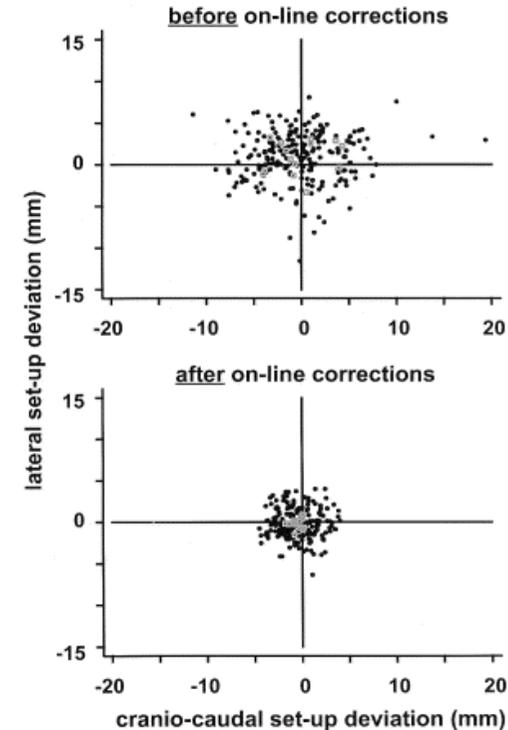
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Incertitudes de positionnement

d in mm	No immobilisation			Alpha cradle mattress			Orfit cast		
	X axis	Y axis	Z axis	X axis	X axis	Z axis	X axis	X axis	Z axis
d ≤ 5	76.5 %	40%	65.5 %	88.5%	79%	100%	84%	84%	97.5%
5 < d ≤ 7.5	12.5 %	23.5 %	73.5 %	7%	13%	0%	15%	16%	2.5%
7.5 < d ≤ 10	4.5%	24%	20%	3.5%	6%	0%	1%	0%	0%
> 10	6.5%	12%	1%	1%	2%	0%	0%	0%	0%
Mean displacement in mm									
	No immobilisation			Alpha cradle mattress			Orfit cast		
X axis	0.7+/- 2.7			0.8+/-1.7			0.3+/-1.4		
Y axis	-5.5+/- 2.6			-2+/-2.7			-0.5+/- 1.1		
Z axis	-0.9+/- 2.2			0.3+/- 0.4			0.5+/- 0.6		

Contention utile mais à discuter au regard de la balance coût-bénéfice

Mitine C et al . *Radiother Oncol* 1999;52:19-27
 Stroom J et al. *IJROBP* 2000;46:499-506



- Procédure de vérification Off-line : 7 to 10 mm
- Procédure de vérification On-line : 3 to 5 mm

Mouvements internes



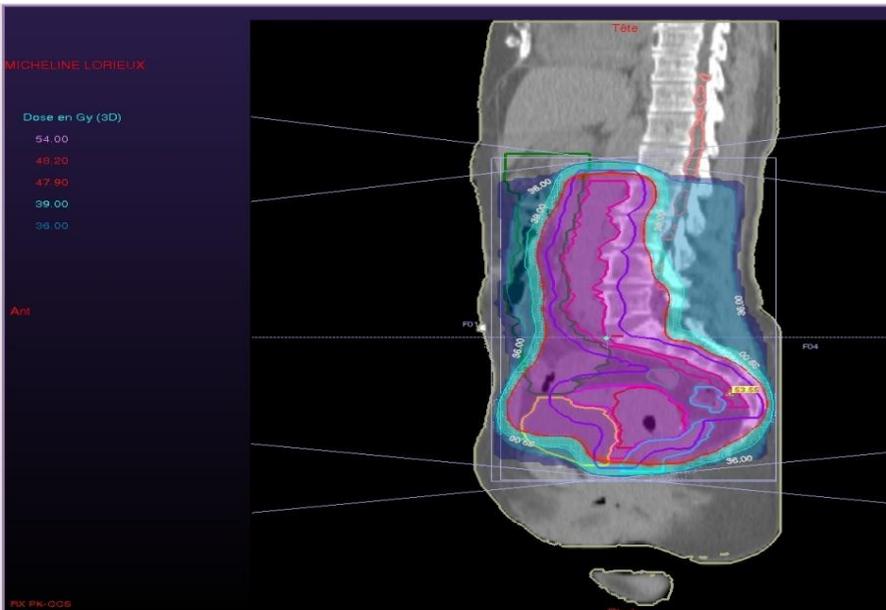
	Differences full vs empty organs		P value
	Median	CI95%	
Cervix lower margin	4 mm	[-1;6]	< 0.05
Corpus ant margin	5 mm	[0;9]	< 0.05
Corpus upper margin	7 mm	[3;15]	< 0.05

Buchali A et al. Radiother Oncol 1999;52:29-34

Margins	GTV	CTV
Ant	12 mm	24 mm
post	14 mm	17 mm
sup	4 mm	11 mm
inf	8 mm	8 mm
Lat right	12 mm	12 mm
Lat left	11 mm	16 mm

Van de Bunt L et al : Radiother Oncol 2008 88;233-240

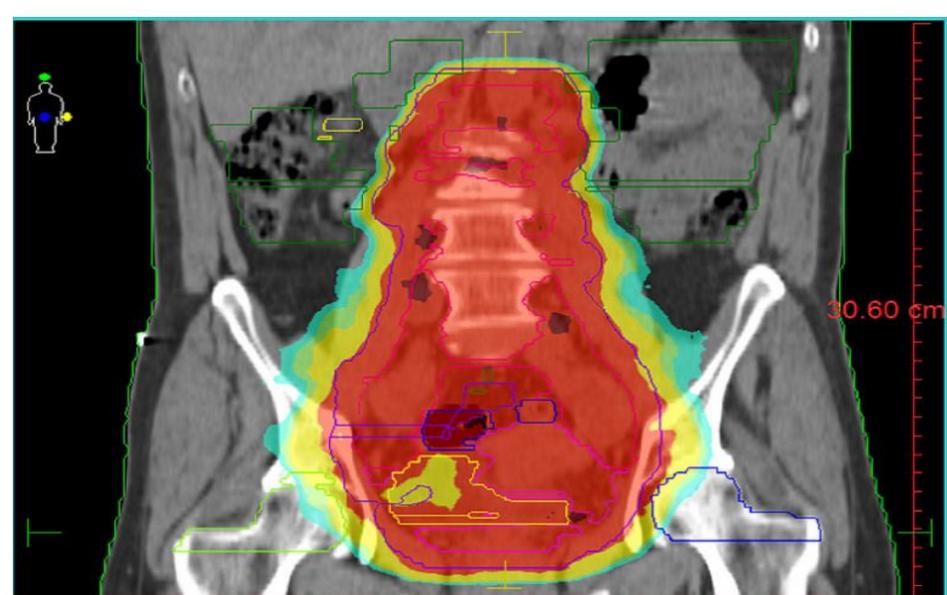
Risque de mauvaise couverture du volume cible



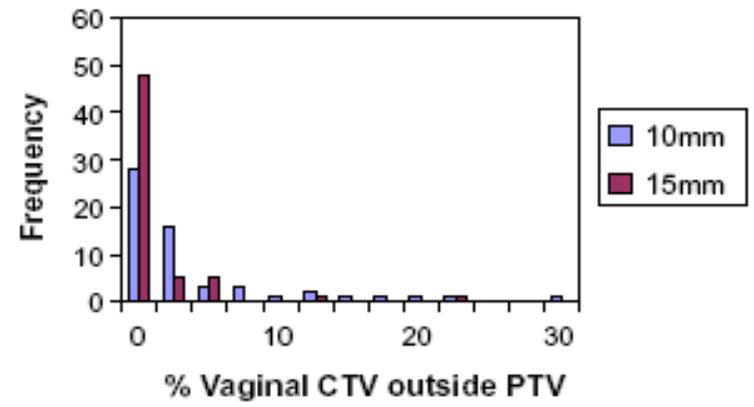
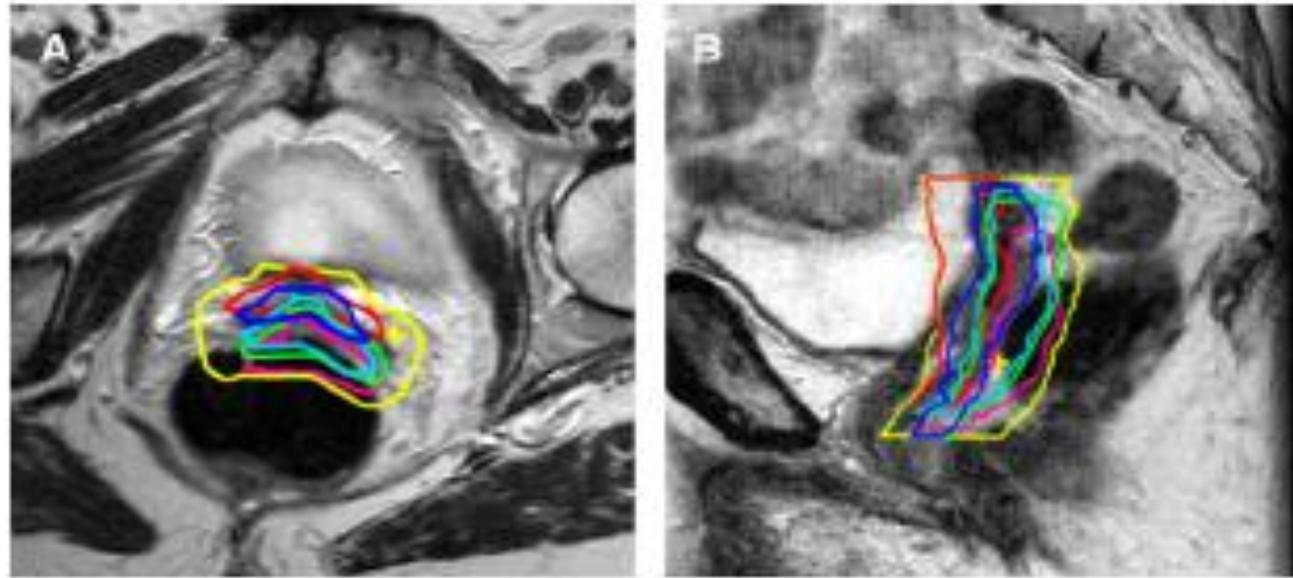
3D



RCMI



Mouvements internes après hystérectomie



- déplacement en antérieur et posterior (max 2,3 cm)
- 1,8 cm en lateral et 1,5 cm en cranio-caudal

Jurgenliemk-schultz I et al : Radiother Oncol 2011;98:244-248

■ ■ ■ ■ Comment prendre en compte les mouvements ?]

- Prévention ?
- Correction ?
- Adaptation ?
-?

■ ■ ■ ■ Prévention : définir des marges adaptées

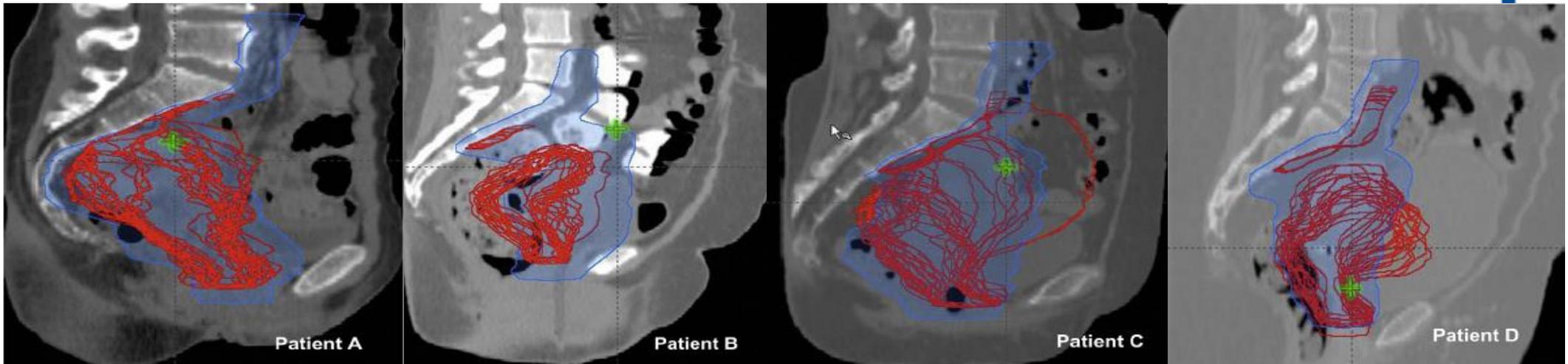


Table 2. Percentage of fractions and volume missed as a function of uniform margin around the clinical target volume

Margin (mm)	Mean % of fractions missing (range)	Mean volume missed (cc) (range)	% of mean volume missed (range)	Mean % of fractions missing (range)	
				Cervical region	Fundus region
0	100 (100–100)	45 (15–112)	10 (3–28)	95 (75–100)	100 (100–100)
3	99 (92–100)	25 (10–84)	6 (2–21)	80 (54–100)	89 (33–100)
5	95 (73–100)	20 (5–72)	4 (1–18)	65 (25–100)	84 (5–100)
7	87 (54–100)	14 (0–62)	3 (0–16)	50 (0–100)	70 (0–100)
10	59 (0–100)	9 (0–46)	2 (0–12)	36 (0–100)	54 (0–96)
15	32 (0–100)	4 (0–21)	1 (0–5)	19 (0–100)	22 (0–73)
20	19 (0–100)	2 (0–8)	0 (0–2)	11 (0–88)	11 (0–58)
25	14 (0–83)	1 (0–4)	0 (0–1)	7 (0–59)	7 (0–33)
30	7 (0–33)	0 (0–2)	0 (0–0)	1 (0–6)	4 (0–17)
35	2 (0–13)	0 (0–1)	0 (0–0)	0 (0–0)	2 (0–13)
40	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)

Tyagi N et al. / Int J Radiat Oncol Biol Phys 2011;80:273-80
 Jadon R et al 2014 Clin Oncol 2014;26:185–96

Prévention : définir des marges adaptées

- Marge du PTV : 15 mm

Marges ≥ 10 mm = Augmentation du volume d'OAR dans le PTV

➔ Réduction de l'impact de la RCMI ?

Table 2. First plans on intratreatment magnetic resonance images*

Average volume in cc	Conventional	Conformal	IMRT
Bowel	601 (115–1456)	425 (53–837)	234 (28–453)
Bladder	92 (19–245)	83 (12–209)	58 (7–115)
Rectum	100 (27–188)	83 (22–156)	75 (20–145)

CTVT au PTVT = 15 mm

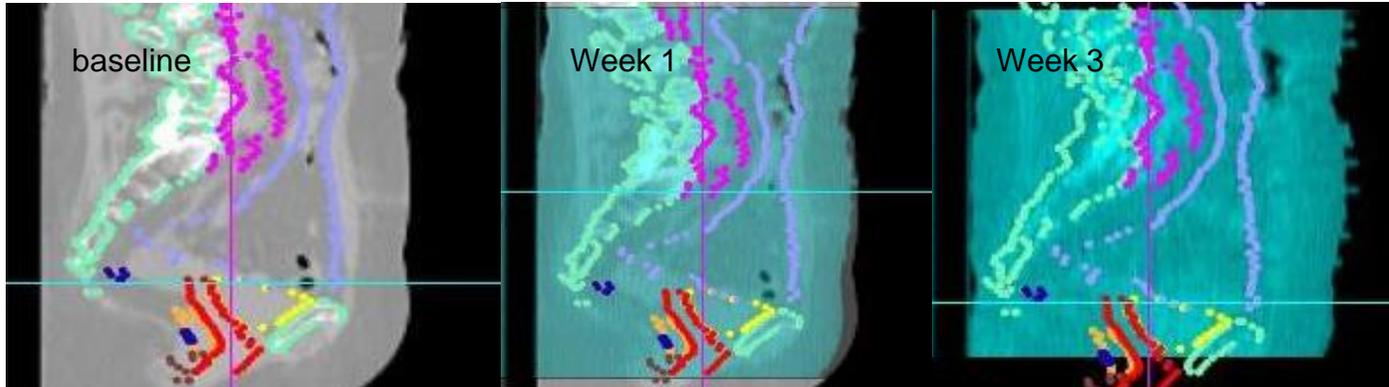
CTVN au PTVN = 10 mm

Abbreviation: IMRT = intensity-modulated radiotherapy.

* Average volumes of the critical organs of all patients receiving 95% of the prescribed dose (range between brackets).

Prévention

- Régime ? Instructions pour le remplissage de la vessie ?

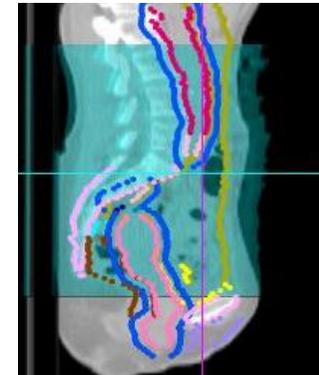
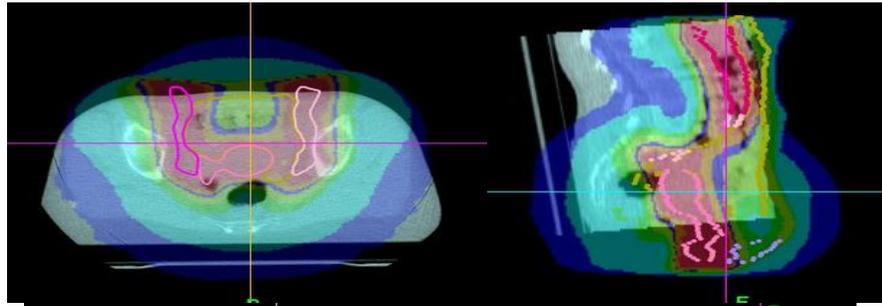
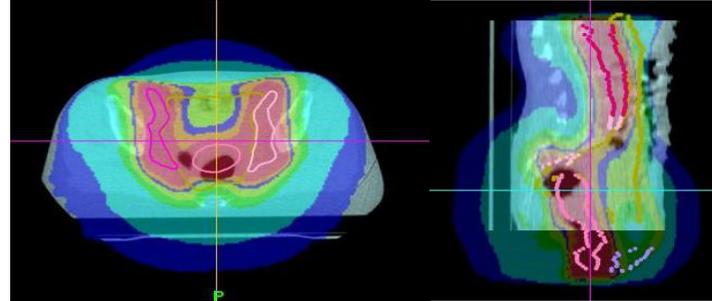
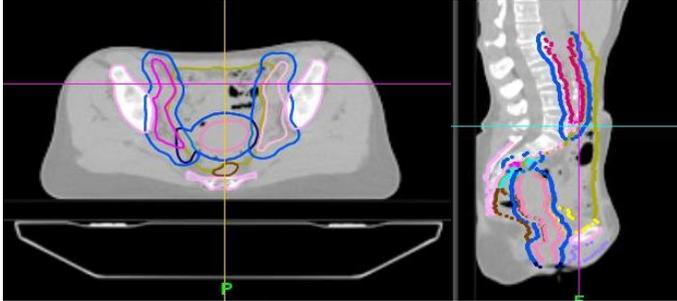


- Le traitement avec la vessie pleine permet de mieux épargner les anses intestinales
Mais: Il est difficile d'obtenir un remplissage vésical constant



Correction = IGRT

- **Correction**



- **Nouvelle installation après passage aux toilettes**

Adaptation= replanification hebdomadaire

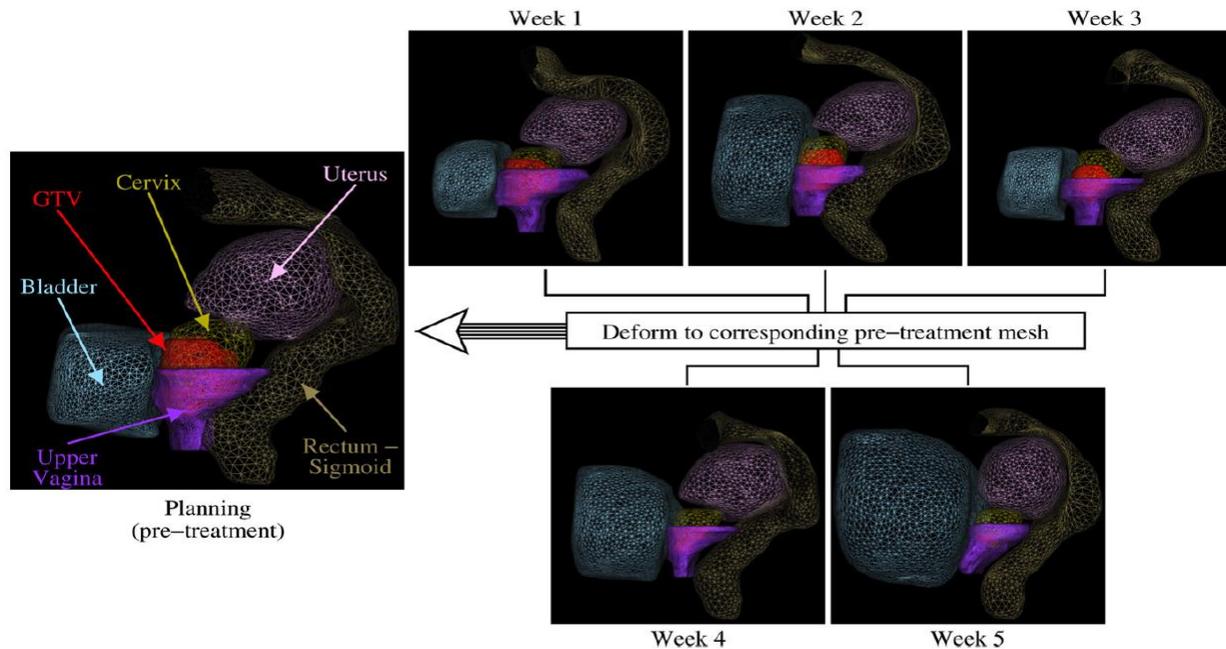


Fig. 2. Sagittal view of surface mesh deformation. Weekly meshes for the bladder, upper vagina, gross tumor volume (GTV), cervix, uterus, rectum-sigmoid, and pelvic bone (not shown) were deformed to their pretreatment mesh to provide an anatomical correspondence between the planning and weekly geometries.

- 15 patientes : la replanification hebdomadaire améliore la couverture des volumes cibles
- Procédure très chronophage pas applicable en routine

Adaptation= Modèle de prédiction des mouvements = bibliothèque de plans

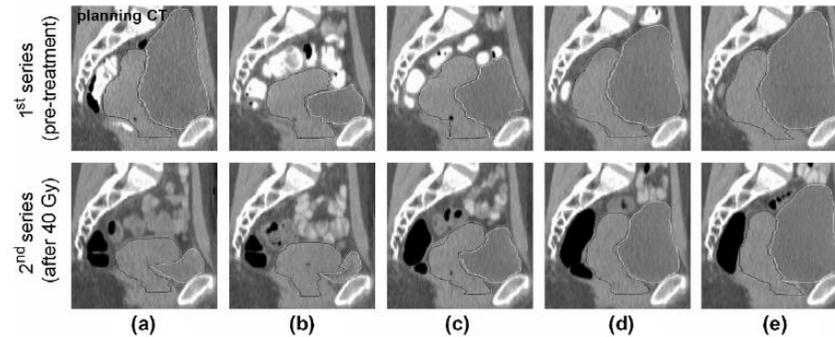


Fig. 1. Variable bladder filling CT-scans (sagittal view) for one patient. Contours: cervix-uterus (black) and bladder (white). First row: pre-treatment series, second row: after-40 Gy series. (a) One hour after drinking 500 ml of water. (b) Empty bladder CT-scan. CT-scans with naturally filling bladder acquired after (c) 20 min, (d) 40 min, (e) 60 min from the acquisition of (b) and drinking 300 ml of water.

Table Margins and corresponding CTV-to-PTV volume for various strategies

Strategy	Description	Margin (mm)	CTV-to-PTV volume (ml)	% Patients with coverage $\geq 95\%$
Full-range mbPTV	Individualized nonadaptive	7	819 \pm 161	90
Library of subrange mbPTVs	Individualized online adaptive			
Two subrange mbPTVs		7	764 \pm 165	90
Three subrange mbPTVs		7	747 \pm 169	90
Daily mbPTVs		10	735 \pm 172	90
Population-based PTV	Population-based nonadaptive			
Large margin		38	1702 \pm 274	90
Small margin		16	831 \pm 172	64

Abbreviations: CTV = clinical target volume; mbPTV = model-based planning target volume; PTV = planning target volume.

Last column indicates the percentage of patients for which at least 95% of the average cervix-uterus volume (over the number of the test computed tomography scans) was inside the PTV.

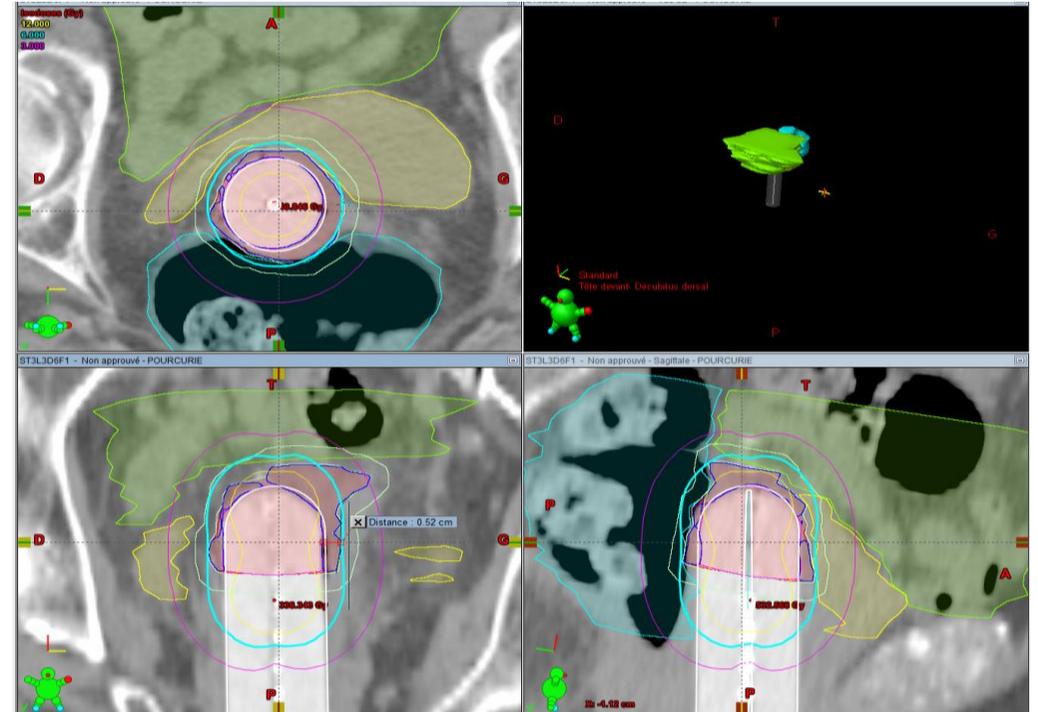
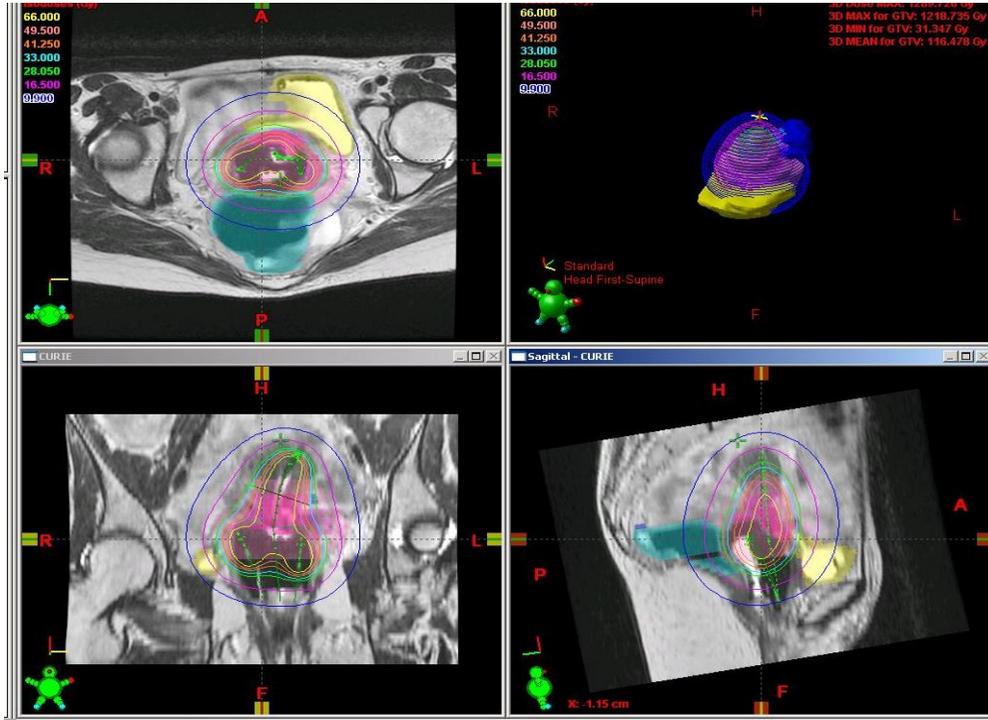
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..... = Curiethérapie



Hypothèse :

La curiethérapie permet de compenser les incertitudes de couverture du volume cible de la RCMI

Compensation de dose de la curiethérapie

- **Cancer du col en place**
 - Marges 15 mm = 20% de risque de mal couvrir le fond utérin = le fond utérin recevra 36 Gy et non pas 45 Gy
 - La curiethérapie utéro-vaginale délivrera 15 Gy au CTV à risque intermédiaire qui comprend le fond utérin
 - Au total le fond utérin recevra $36+15= 51$ Gy
- **Voute vaginale en post-opératoire**
 - Marges 15 mm = 5 % de risque de mauvaise couverture= la voute recevra 42 Gy au lieu de 45 Gy
 - La curiethérapie de la voute délivrera une dose eqD2Gy dose of 10 Gy
 - Au total la voute recevra $42+ 10= 52$ Gy



La radiothérapie en conditions stéréotaxiques

Place de la stéréotaxie : récurrence ganglionnaire

- 30 patientes ayant présenté une récurrence lombo-aortique isolée après traitement pelvien initial d'un cancer du col (28 patientes) ou de l'endomètre (2 patientes).
- Temps moyen de survenue 22 mois (3-81mois)
- 2 patientes ont reçu une chimiothérapie néo-adjuvante, 9 une chimiothérapie concomitante et 14 une chimiothérapie adjuvante

Table 2. Radiation dose and estimated conventional radiation therapy dose

Radiation dose (Gy)		Fractions of SBRT	No. of patients	PTV (ml)	NTD _{2Gy}
EBRT	SBRT				
45	13	1	1	7.4	60
27-45	30-33	3	3	5.5-54.2	77-94
	33-37.5	3	12	3.7-52.5	58-70
	39	3	11	5.6-57.3	75
	42-45	3	3	1.3-7.7	84-94

Abbreviations: EBRT = external beam radiation therapy; NTD_{2Gy} = normalized total dose in 2-Gy fraction; PTV = planning target volume; SBRT = stereotactic body radiation therapy.

Table 3. Chemotherapy regimen

Regimen	No. of patients
Paclitaxel, cisplatin	16
Topotecan, cisplatin	3
5-Fluorouracil, cisplatin	3
Irinotecan, cisplatin	1
Cisplatin, adriamycin, paclitaxel	1
Cisplatin	1
None	5

Place de la stéréotaxie : récurrence ganglionnaire

- 15 mois de recul médian
- A 4 mois après traitement 65,5% de RC, 31% de RP, 3,5% perdu de vue
- Résultats non influencés par l'âge, le délai d'apparition de la récurrence, la dose pondérée à 2 Gy/fraction supérieure ou inférieure à 70 Gy, la chimiothérapie
- Influence péjorative du volume tumoral si supérieur à 17 cc (ganglion de 3 cm) sur le contrôle local et la survie sans progression.
- Toxicité hématologique de grade 3 seulement chez 5 patientes, 1 sténose urétérale

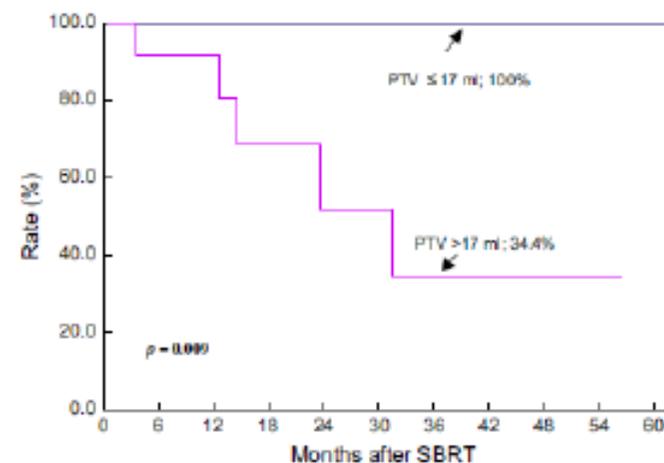
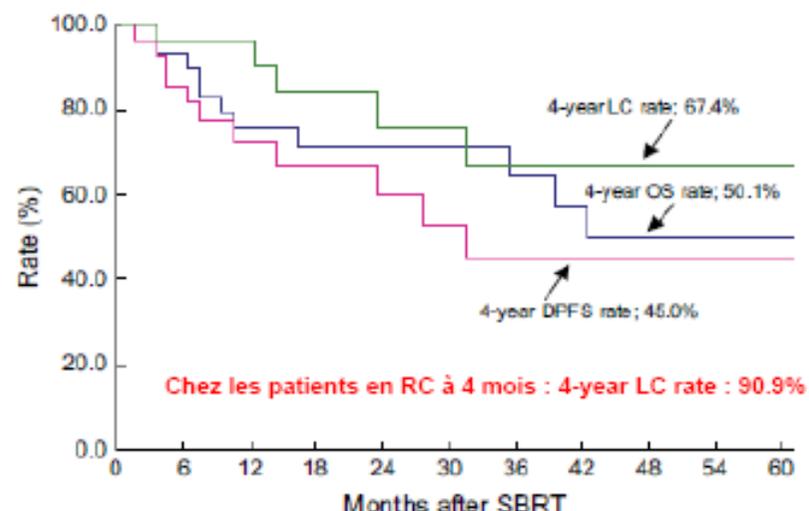


Fig. 5. Four-year local control (LC) rate according to planning target volume (PTV). Of the patients, 16 had PTVs ≤ 17 ml and the remaining 13 patients had PTVs > 17 ml.

Conclusions

- La RCMI doit être considérée comme la technique standard d'irradiation des cancers gynécologiques si
 - Elle est suivie de curiethérapie
 - Les marges CTV-PTV ne sont pas réduites
 - L'IGRT est utilisée de façon adaptée
- La participation à des études prospectives doit toujours être encouragée
- La radiothérapie adaptative devrait permettre de minimiser la mauvaise couverture du volume cible. Elle devrait permettre de réduire les marges et de mieux protéger les OAR
- L'irradiation en condition stéréotaxique a certainement une place à trouver dans le cadre de l'escalade de dose au niveau des ganglions envahis.