

Injections intra-caverneuses et vacuum après prostatectomie radicale

Pr René Yiou

Service d'urologie

CHU Henri Mondor Créteil

Réhabilitation sexuelle

- Définition¹: « *SR after RP consists in the use of any drug or device to maximize recovery of functional erections* »
- Concept introduit par Montorsi (1997) avec les injections intra-caverneuses (IIC) d'alprostadil:
 - Erections spontanées à 6 mois: 67% vs 20% si pas d'IIC
- PDE5i: actuellement traitement de référence¹
 - Tx d'abandon 78% à 18 mois pour manque d'efficacité²
 - ➔ Les IIC restent d'actualité: si échec PDE5i, PR non conservatrice

Injections intra-caverneuses

Alprostadil: Edex, Caverject Dual

Trimix (Hors AMM) : Alprostadil (10 mg/mL)+
phentolamine (1 mg/mL) + papaverine (30 mg/mL)

- Efficacité à long terme et améliore la vascularisation pénienne dans d'autres DE
- A l'origine du concept de réhabilitation sexuelle après PR. Mais :
 - effets à long terme en cas de PR restent mal connus
 - douleur en cas de PR: physiopathologie mal connue et traitement mal codifié

Taux de récupération d'érections spontanées sous IIC

<i>Author(s)</i>	<i>Reference</i>	<i>Drug(s) used</i>	<i>% of patients not requiring any injections</i>	<i>% of patients requiring reduced frequency or dose</i>	<i>Number of patients</i>
Buvat <i>et al</i>	<i>W J Urol</i> 1987; 5 : 150	Papaverine	28%	NA	47
Lakin <i>et al</i>	<i>J Urol</i> 1990; 143 : 1138	PPV ± Phent	3%	NA	100
Virag <i>et al</i>	<i>J Urol</i> 1991; : 287	PPV ± Phent, 6 drugs	15%	50%	615
Bennett <i>et al</i>	<i>J Urol</i> 1991; 146 : 1564	PPV, Phent + PGE	2%	NA	116
Kerfoot and Carson	<i>J Urol</i> 1991; : 1022	PPV + Phent	5%	NA	119
Gerber and Levine	<i>J Urol</i> 1991; 146 : 786	PGE	6%	NA	72
Speranza and Ruiz	<i>IJIR</i> 1992; 4 Suppl 2: 109	PPV ± Phent, PGE	11%	1%	412
Hollander <i>et al</i>	<i>Urol</i> 1992; 439	PPV + Phent or PGE	5%	NA	115
McMahon	<i>IJIR</i> 1992; 4 179	PGE	9%	NA	116
Basile <i>et al</i>	<i>IJIR</i> 1994; 6 Suppl 1: D118	Not stated	6%	32%	334
Weiss <i>et al</i>	<i>IJIR</i> 1994; 6 171	PPV/Phent or PGE	8%	NA	140
Marshall <i>et al</i>	<i>Urol</i> 1994; 43 : 844	PGE or Trimix	3%	35%	35
Vardi <i>et al</i>	<i>IJIR</i> 1996; 8 :114 Abst A61	PGE, PPV/Phent, Trimix	6%	NA	450
Tu <i>et al</i>	<i>IJIR</i> 1996; 8 : 112 Abst A55	PGE	37%	NA	16
Buvat <i>et al</i>	<i>IJIR</i> 1996; 8 : 41	PGE	9%	10%	130
Total			2–37%	1–50%	2817

Does natural erectile function improve following intracavernous injections of vasoactive drugs? *Int J Impot* (2007)

Les IIC améliorent la vascularisation pénienne

Repeated intracorporeal self-injection: effect on peak systolic velocity and cavernosal artery diameter. Awad et al. International Journal of Impotence Research (2007)

- 60 patients traités avec mélange de drogues,
- 2^e évaluation après 10^e injection

Table 1 Comparison of PPDU parameters at the start and end of the study

<i>PPDU parameter</i>	<i>At the beginning</i>	<i>At the end</i>
Rt Cav. A diameter (mm) (before ICI)	0.64 ± 0.13	0.81 ± 0.22*
Rt Cav. A diameter (mm) (after ICI)	0.63 ± 0.12	0.79 ± 0.22*
Lt Cav. A diameter (mm) (before ICI)	1.01 ± 0.18	1.34 ± 0.39*
Lt Cav. A diameter (mm) (after ICI)	1.09 ± 0.19	1.27 ± 0.33*
Rt Cav. A PSV (cm/sec)	33.77 ± 13.26	44.4 ± 1.19*
Lt Cav. A PSV (cm/sec)	32.33 ± 8.09	46.1 ± 5.86*

*Significant at $P < 0.001$.

Satisfaction des IIC à long terme

Intracavernous Injections of Prostaglandin E1 for Erectile Dysfunction: Patient Satisfaction and Quality of Sex Life on Long-Term Treatment.
Alexandre et al. J sex Med 2007
N=506, 35 mois de recul

On the whole, are you satisfied with ICI? (N = 589)

Very satisfied	33.2 ± 0.038
Moderately satisfied	45.1 ± 0.040
Neither satisfied nor dissatisfied	12.0 ± 0.026
Moderately dissatisfied	3.5 ± 0.015
Very dissatisfied	5.9 ± 0.019

Are you prepared to continue ICI? (N = 587)

Certainly	64.6 ± 0.039
Fairly certainly	18.7 ± 0.032
Don't know	11.8 ± 0.026
Probably not	2.2 ± 0.012
Very probably not	2.7 ± 0.013

How confident has ICI made you with regard to intercourse? (N = 587)

Very confident	34.1 ± 0.038
Moderately confident	46.2 ± 0.040
No change	11.2 ± 0.026
Not very confident	6.3 ± 0.020
Not at all confident	2.2 ± 0.012

Since you began ICI, have you noted any changes in:

	<i>Your sex life (N = 575)</i>
Not as good	16.5 ± 0.030
Unchanged	13.4 ± 0.028
Rather better	70.1 ± 0.037

Efficacité à long terme des mélanges après prostatectomie radicale

The Use of an Erectogenic Pharmacotherapy Regimen Following Radical Prostatectomy Improves Recovery of Spontaneous Erectile Function. Mulhall J Sex Med 2005

- Protocole de réhabilitation sexuelle: Viagra 100x4 si échec: Trimix ou Bimix si douleur, puis nouveau test Viagra/4 mois

Table 3 Postoperative erectile function outcomes at 18 months

	Rehabilitation group (n = 58)	No rehabilitation group (n = 74)	P value
Patients with functional erections (nonmedication assisted) [†]	52%	19%	<0.001*
Patients responding to sildenafil [‡]	64%	24%	<0.001*
Patients responding to intracavernosal injections [‡]	95%	76% [§]	<0.01*

* Mann–Whitney *U*-test for difference between *rehabilitation* and *no rehabilitation* groups.

[†] Functional erections permitting sexual intercourse ($\geq 60\%$ rigidity) unassisted by medication.

[‡] Response defined as ability to achieve vaginal penetration.

[§] Of the 32 patients in the *no rehabilitation* group who attempted injection therapy by 18 months.

Importance du suivi thérapeutique

Sexual Counseling Improved Erectile Rehabilitation After Non-Nerve-Sparing Radical Retropubic Prostatectomy or Cystectomy—Results of a Randomized Prospective Study. Titta et al. J Sex Med 2006

- Prostatectomie radicale non conservatrice
- Dose de départ: 10 µg alprostadil. Tous les patients répondeurs au départ

Résultats:

- Douleur sévère (13%) ou modérée (34%)
- **Sexual Counselling (n=29) > non-SC (28) pour l’IEEF-EF et la réponse au Sildénafil à 18 mois**

Table 1 IIEF mean scores in home ICI therapy

	Before surgery		Before ICI		3rd month		18th month	
	SC+	SC-	SC+	SC-	SC+	SC-	SC+	SC-
Erectile function	26.6	26.1	8.4	8.4	23.4	21.7	26.5	24.3
Sexual satisfaction	10.2	10.2	3	3	8.3	8	9.7	6.8
Orgasmic function	10	9.4	3.3	3.4	8.7	7.5	9.2	7.8
Sexual desire	8.7	8.5	8.5	8.5	8.4	6.5	9	6.2
Overall satisfaction	9.2	9.1	6.2	7.4	7.7	7.4	9.0	7.3

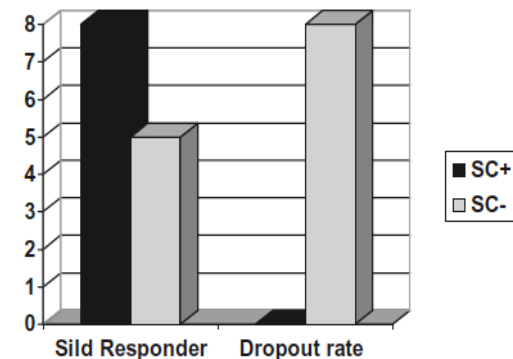


Figure 1 Home Sildenafil responders rate and dropout rate.

La douleur post-injection diminue avec le temps mais altère le processus de réhabilitation sexuelle

Table 1 Mean International Index of Erectile Function (IIEF) scores, Erection Hardness Scores (EHS), and penile pain scores with and without intracavernous alprostadil injections (IAI) after bilateral nerve-sparing radical prostatectomy

N = 87	Month 6	Month 12	P value
Alprostadil dose injected (μ g)	8.05 \pm 5.28	9.91 \pm 8.15	NS
Number of injections/week	1.89 \pm 0.46	1.72 \pm 0.55	NS
Pain related to the injection	1.87 \pm 2.1	1.78 \pm 2.3	NS
Pain during erection	3.2 \pm 2.45	2.49 \pm 2.46	0.03
IIEF erectile function score with IAI	14.06 \pm 10.89	17.15 \pm 11.01	0.03
IIEF erectile function score without IAI	4.56 \pm 4.08	5.44 \pm 5.45	NS
IIEF orgasmic function score with IAI	4.06 \pm 3.39	4.86 \pm 3.45	NS
IIEF orgasmic function score without IAI	2.08 \pm 2.52	2.58 \pm 2.87	NS
IIEF sexual desire score	5.78 \pm 2.07	5.75 \pm 2.41	NS
IIEF intercourse satisfaction score	5.22 \pm 4.47	6.03 \pm 4.61	NS
IIEF overall satisfaction score	5.04 \pm 2.54	5.34 \pm 2.77	NS
EHS with IAI	2.52 \pm 1.26	2.72 \pm 1.35	NS
EHS without IAI	0.43 \pm 0.77	0.9 \pm 1.01	0.001

The data are mean \pm SD.

IIEF = International Index of Erectile Function; EHS = Erection Hardness Score; IAI = Intracavernous alprostadil injection.

Sexual Rehabilitation and Penile Pain Associated with Intracavernous Alprostadil after Radical Prostatectomy. Yiou et al. J Sex Med 2011

Vacuum

- Mécanisme d'action:
 - Augmentation du flux artériel,
 - Anneau constricteur réduit le retour veineux
 - Etudes animales ¹: diminution TFG b-hypoxie, augmentation ratio muscle lisse/collagène et NOSe
- Etudes randomisées.
 - Initiation précoce (1 mois)
 - Préservation longueur pénienne
 - Tx abandon élevé
 - TTT de 1ere ligne?
- Effets secondaires: Douleurs, froideur
- CI: tb hémostase, priapisme

Vacuum

Table 5 Post radical prostatectomy

First author	Year	Population studied	N	Modality	VED efficacy findings
Köhler	BJU Int 2007	1 month after RP (Group 1) or 6 months after RP (Group 2)	28	VED	<ul style="list-style-type: none"> In men who started VED at 1 month after RP IIEF-EF was 11.5 after 3 months and 12.4 at 6 months In men who started VED at 6 months after RP IIEF-EF was 1.8 and 3.0 after 3 and 6 months, respectively Stretched penile length was preserved in Group 1 and significantly decreased by approximately 2 cm in Group 2
Raina	Int J Impot Res 2006	RP patients who subsequently developed ED	109	VED or observation alone	<ul style="list-style-type: none"> 80% used their VED at a frequency of 2 times per week with a spousal satisfaction rating of 55%
Zippe	Curr Urol Rep 2008	Patients after NSRP	60	VED vs. no VED	<ul style="list-style-type: none"> In compliant men, 23% reported decrease in length and girth vs. 63% in the non-VED user group after 9 months of use 80% of compliant men reported a quicker return to sexual activity
Dalkin	Int J Impot Res 2007	Men with good preoperative function after NSRP	42	VED	<ul style="list-style-type: none"> In those who used the device 50% or more of the time, only 1/36 (3%) had a decrease of less than or equal to 1.0 cm
Gontero	BJU Int 2005	Potent men after NNSRP	76	Consecutive treatment of sildenafil then VED and other ED treatments	<ul style="list-style-type: none"> 52% were considered responders to VED At 1 year 20% were still using erectile aids
Engel	Can J Urol 2011	Men with prostate cancer after bilateral nerve-sparing robotic prostatectomy	23	Tadalafil or tadalafil + daily unbanded VED	<ul style="list-style-type: none"> IIEF-5 was significantly higher for combination group at 6, 9, and 12 months Penile hardness scores were significantly greater at 6 and 9 months At 12 months 92% of combination patients responded yes to the vaginal penetration question (SEP2) compared with 57% who used tadalafil only At 12 months 92% of combination patients responded yes to the intercourse to organism question (SEP3) compared with 29% who used tadalafil only
Baniel	BJU Int 2001	Men undergoing RRP	85	Progressive ED treatments, starting with VED	<ul style="list-style-type: none"> 92% responded to the VED with an erection sufficient for vaginal penetration 14% agreed to continue it at home

ED = erectile dysfunction; IIEF-EF = International Index of Erectile Function-erectile function domain; IIEF-5 = International Index of Erectile Function—5 Questionnaire (SHIM); NNSRP = non-nerve-sparing radical prostatectomy; NSRP = nerve-sparing radical prostatectomy; RP = radical prostatectomy; RRP = retropubic radical prostatectomy; SEP-2 = Sexual Encounter Profile question 2; SEP-3 = Sexual Encounter Profile question 3; VED = vacuum erection device