
Erectile dysfunction: Radiation Therapy

Filippo Alongi, MD, PhD

Chair of Radiation Oncology Department
Sacro Cuore Don Calabria Hospital,
Negrar-Verona, Italy



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Background

Definition

Erectile dysfunction (ED) is [sexual dysfunction](#) characterized by the inability to develop or maintain an [erection](#) of the [penis](#) during [sexual activity](#)

DSM-IV, American Psychiatric Association, 1994

NIH Consensus Development Panel on Impotence, JAMA, 270:83, 1993

[J Urol](#). 1994 Jan;151(1):54-61.

Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study.

[Feldman HA](#)¹, [Goldstein I](#), [Hatzichristou DG](#), [Krane RJ](#), [McKinlay JB](#).

The combined prevalence of minimal, moderate and complete **impotence was 52%**. The prevalence of complete impotence tripled from 5 to 15% between subject ages 40 and 70 years. **Subject age was the variable most strongly associated with impotence.**



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Background

Risk factors

! Psychological factors

! Age

! Physical activity

! Medications

! Tobacco

! Alcohol

! Drug use

! Dyslipidemia

! Trauma

! Pelvic surgery

! Cardiovascular disease

! Diabetes mellitus

! Liver disease

! Nephropathy

! Neurological Disorders

! Hormonal disorders

! Respiratory diseases

! Neuropsychiatric diseases



Background

Risk factors

REVIEW ARTICLE

Epidemiology of sexual dysfunction in the male population

M. E. Beutel¹, W. Weidner² & E. Brähler³

Andrologia **38** (2006) 115–121

Prevalence of erectile dysfunction according to age group

30–39 years: 2.3%^a

40–49 years: 0%^b to 9.5%^a

50–59 years: 2%^b to 15.7%^a and 30.8%^c

60–69 years: 11%^b to 23%^d, 34.4%^a and 55.1%^c

>70 years: 15% (70–75 years^e) to 40%^b

70–79 years: 47%^d to 53.4%^a

80 years and above: 64%^d to 76% (70–80 years^c)

^aBraun *et al.* (2000).

^bHolden *et al.* (2005).

^cRosen *et al.* (2003).

^dBacon *et al.* (2003).

^eFeldman *et al.* (1994).

Background

Risk factors

Diabetes mellitus : Erectile dysfunction (DE) $\pm$ 50% (range 20 – 75%)

Melman A & Gingell JC, J Urol, 161(1):5-11, 1999

Cardiovascular disease (ipertension, reduction of tissue oxigenation): DE: 46 %

Roth et al. Clin Cardiol 26:25-30, 2003

Nephropathy : DE: 86.4 %

Complete 25.4%, moderate 35.4%, mild 24.6%

Neto et al. Int J Impot Res 14 (Supl.2):S19-24, 2002

Alcool: >600ml per week, risk of **DE: 17 a 29%**

Feldman HA et al, J Urol, 151:54, 1994

Prevalence of DE in prostate cancer patients

Prevalence of Baseline Erectile Dysfunction (ED) in an Australian Cohort of Men with Localized Prostate Cancer

Wee Loon Ong, MBBS,*† Hamish McLachlan, MBBS,* and Jeremy L. Millar, MBChB*†

Results. Prior to permanent seed brachytherapy, 335 (48%) patients reported no ED, 129 (17%) mild ED, 42 (6%) mild–moderate ED, 37 (5%) moderate ED, and 165 (24%) severe ED. In multivariate analyses, age, diabetes, and hypertension remained to be independently associated with ED, with diabetes most strongly associated with worse ED (odds ratio = 2.6; 95% confidence interval = 1.3–5.3).

J Sex Med. 2015 Apr 1. doi: 10.1111/jsm.12867

Risk of DE for treatment of prostate cancer patients

Radiotherapy

Erectile dysfunction (ED) post-RT: 6-60% (partial or complete)

Etiology: - probably penile bulb dose
- psychological factors
- neuro-vascular damage

74-80% of cases: improvements with medications

Zelevsky, IJROBP 1998
DiBiase, IJROBP 2000
Stock, J Urol 2001
Incrocci9, IJROBP 2002
Wust, radiat Oncol 2004
Merrick, IJROBP 2005
Stone, Urol 2007

Risk of DE for treatment of prostate cancer patients

Surgery



Urinary Incontinence and Erectile Dysfunction After Robotic Versus Open Radical Prostatectomy: A Prospective, Controlled, Nonrandomised Trial

Eva Haglind^{a,*}, Stefan Carlsson^b, Johan Stranne^c, Anna Wallerstedt^b, Ulrica Wilderäng^d, Thordis Thorsteinsdottir^{d,e}, Mikael Lagerkvist^f, Jan-Erik Damber^c, Anders Bjartell^g, Jonas Hugosson^c, Peter Wiklund^b, Gunnar Steineck^{d,h},
on behalf of the LAPPRO steering committeeⁱ

EURURO-6097; No. of Pages 10

ARTICLE IN PRESS

EUROPEAN UROLOGY XXX (2015) XXX–XXX

Definition of erectile dysfunction	Open surgery, n (%)	Robot-assisted surgery, n (%)	Adjusted A, OR (95% CI) **	Adjusted B, OR (95% CI) †	Adjusted C, OR (95% CI) ‡
IIEF score §	531 (75)	1200 (70)	0.80 (0.64–1.00)	0.79 (0.63–1.00)	0.73 (0.58–0.93)
IIEF-5 score # at 12 mo ≤16	570 (81)	1311 (78)	0.86 (0.68–1.09)	0.75 (0.58–0.96)	0.75 (0.58–0.97)
IIEF-5 score # at 12 mo ≤21	654 (93)	1508 (90)	0.71 (0.50–0.99)	0.61 (0.42–0.88)	0.61 (0.42–0.88)
Penile stiffness less than half of the time	574 (81)	1323 (77)	0.81 (0.64–1.03)	0.75 (0.59–0.96)	0.75 (0.58–0.97)
No spontaneous morning erection	664 (93)	1522 (89)	0.59 (0.42–0.82)	0.52 (0.36–0.76)	0.50 (0.35–0.74)
Erectile dysfunction, combined variable +	561 (79)	1282 (75)	0.80 (0.64–1.00)	0.74 (0.59–0.95)	0.75 (0.58–0.96)



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Risk of DE for treatment of prostate cancer patients

Surgery



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EURURO-6097; No. of Pages 10

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EUROPEAN UROLOGY XXX (2015) XXX–XXX

Results and limitations: Of 2625 eligible men, 2431 (93%) could be evaluated for the primary end point. At 12 mo after RALP, 366 men (21.3%) were incontinent, as were 144 (20.2%) after RRP. The adjusted OR was 1.08 (95% confidence interval [CI], 0.87–1.34). Erectile dysfunction was observed in 1200 men (70.4%) 12 mo after RALP and 531 (74.7%) after RRP. The adjusted OR was 0.81 (95% CI, 0.66–0.98). The frequency of positive surgical margins did not differ significantly between groups: 21.8% in the RALP group and 20.9% in the RRP group (adjusted OR: 1.09; 95% CI, 0.87–1.35). The non-randomised design is a limitation.

Conclusions: In a Swedish setting, RALP for prostate cancer was modestly beneficial in preserving erectile function compared with RRP, without a statistically significant difference regarding urinary incontinence or surgical margins.



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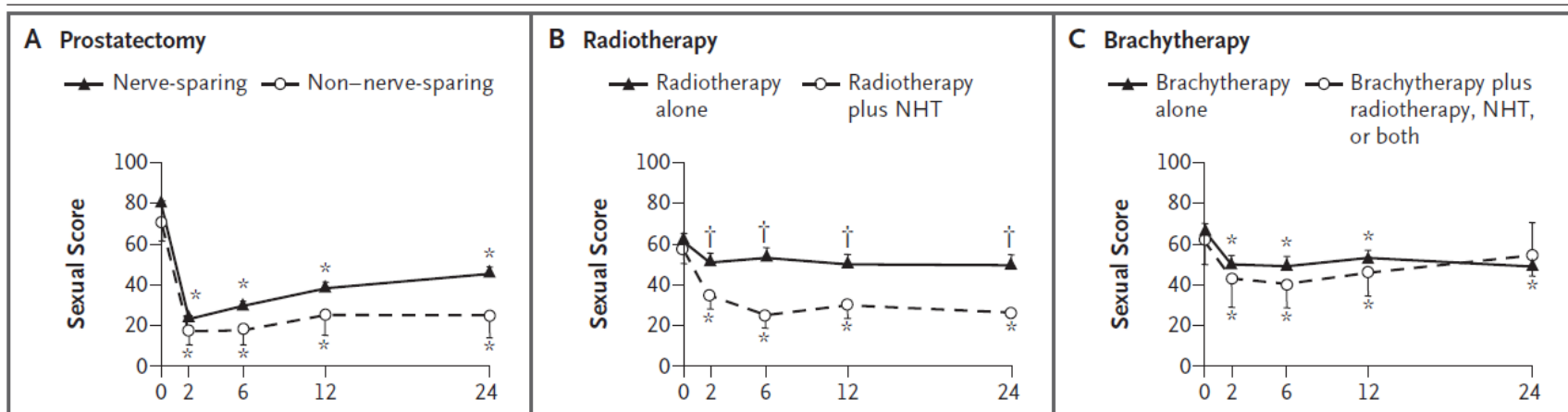
Surgery vs Radiotherapy

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

N Engl J Med 2008;358:1250-61.

Quality of Life and Satisfaction with Outcome among Prostate-Cancer Survivors



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Quality of Life and Satisfaction with Outcome among Prostate-Cancer Survivors

Table 2. Percent of Patients Reporting Specific Levels of Distress or Dysfunction for Each Quality-of-Life Domain, as Queried on the EPIC-26 Survey.*

Quality-of-Life Domain and EPIC Questionnaire Item	Prostatectomy					External-Beam Radiotherapy					Brachytherapy				
	Baseline (N=603)	2 Mo (N=571)	6 Mo (N=573)	12 Mo (N=557)	24 Mo (N=372)	Baseline (N=292)	2 Mo (N=276)	6 Mo (N=264)	12 Mo (N=258)	24 Mo (N=178)	Baseline (N=306)	2 Mo (N=286)	6 Mo (N=288)	12 Mo (N=272)	24 Mo (N=180)
<i>percent</i>															
Sexual function															
Poor erections	14	88	80	67	58	37	52	56	57	60	30	51	50	48	51
Difficulty with orgasm	12	62	51	45	42	32	47	53	52	50	24	49	44	38	45
Erections not firm†	17	90	84	75	64	48	63	62	64	66	36	58	58	54	56
Erections not reliable‡	10	83	75	60	51	30	46	48	51	51	24	42	47	40	44
Poor sexual function	12	83	74	61	53	34	50	54	53	58	28	47	48	43	46
Overall sexuality problem†	12	59	59	50	43	18	28	30	29	37	18	34	34	29	30



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N Engl J Med 2008;358:1250-61.

Table 4. Problems Reported by 543 Patients and Their Partners Regarding Symptoms and the Association between Changes in Patients' Quality-of-Life Scores and Levels of Distress Reported by Their Partners 1 Year after Treatment.*

Quality-of-Life Domain and Reported Level of Domain-Specific Distress	Patient			Spouse or Partner			Association between Change in Patient's Quality of Life and Distress for Partner			
	Prosta-tectomy	Radio-therapy	Brachy-therapy	Prosta-tectomy	Radio-therapy	Brachy-therapy	Prosta-tectomy	Radio-therapy	Brachy-therapy	All Groups
	number (percent)			number (percent)			correlation coefficient			
Sexual function							0.35†	0.11	0.22‡	0.36†
No. of responses	268	113	116	279	126	122				
No problem or very small problem	78 (29)	53 (47)	61 (53)	114 (41)	83 (66)	83 (68)				
Small problem	55 (21)	25 (22)	20 (17)	42 (15)	16 (13)	23 (19)				
Moderate problem	65 (24)	17 (15)	16 (14)	65 (23)	15 (12)	9 (7)				
Big problem	70 (26)	18 (16)	19 (16)	58 (21)	12 (10)	7 (6)				



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Radiotherapy

REVIEW ARTICLE

(Am J Clin Oncol 2009;32: 443–447)

Erectile Dysfunction After Radiotherapy for Prostate Cancer

William M. Mendenhall, MD,† Randal H. Henderson, MD, MBA,*† Daniel J. Indelicato, MD,*†
Sameer R. Keole, MD,*† and Nancy P. Mendenhall, MD*†*

TABLE 1. Metaanalysis of the Probability of Maintaining Erectile Function After Treatment for Localized Prostate⁹

Treatment	No. Patients	~1 Yr Post-Rx (%)	No. Patients	~2 Yrs Post-Rx (%)	Age Adjusted (%)
BT alone	172	76	No data	No data	80
BT + EBRT	58	60	58	60	69
EBRT	1343	55	731	52	68
RP-					
-Nerve sparing	485	34	128	25	22
-Standard	3019	25	2673	25	16
Cryotherapy	264	13	198	15	13

EBRT, external beam radiotherapy; RP, radical prostatectomy; Rx, treatment.



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Radiotherapy

Radiotherapy and Oncology 93 (2009) 153–167



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journal homepage: www.thegreenjournal.com



Systematic review

Sexual function

Erectile dysfunction: dose–volume relationships

Due to the growing proportion of potent patients before radiotherapy of prostate cancer and the widespread availability of anti-impotence drugs, the exclusion of structures potentially involved in penile erection (bulb of the penis, neurovascular bundles, crura, corpora cavernosa) from the irradiated volume is a very sensitive and controversial topic. Recently, some studies have reported a correlation between the dose received by penile structures (mostly the penile bulb) and sexual function alterations (mostly impotence) [140–145].

In particular, a median dose to the penile bulb greater than 52 Gy was found to be highly correlated with an increased risk of erectile dysfunction (ED) [145]. Other authors have reported results consistent with this finding: Wernicke et al. [144] suggested keeping V50Gy < 20% and V40Gy < 40% to drastically reduce impotence. Mangar et al. [143] reported a median bulb dose of 59.2 and

45.5 Gy for impotent and potent men, respectively, in a cohort of 51 patients included in a randomized trial. However, other investigators found no clear dose–volume effect [146–148]; a more complete review can be found in [4].

The wide use of hormonal therapy and of anti-impotence drugs suggests that large prospectively questionnaire-based scored populations would be necessary to reliably assess dose–volume relationships taking into account pre-treatment erectile status and impact of both hormonal therapy and anti-impotence drugs; this point will be discussed in the next section.

In any case, based on the available literature data, sparing the bulb, even partially, without compromising the coverage of the PTV, may be suggested: in particular, the use of MRI to better define the prostate apex in potent patients with prostate cancer may safely spare the bulb of the penis without missing the prostate in most patients [149–152].



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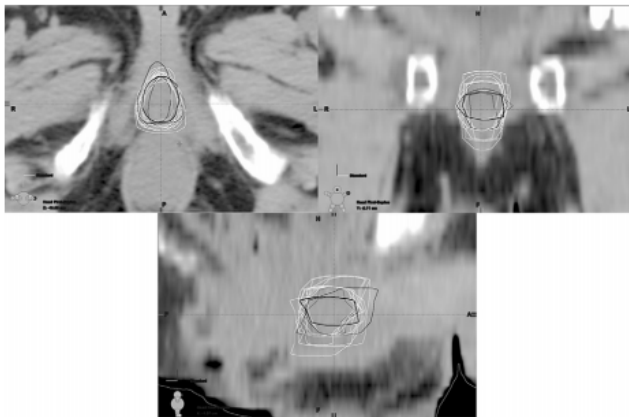
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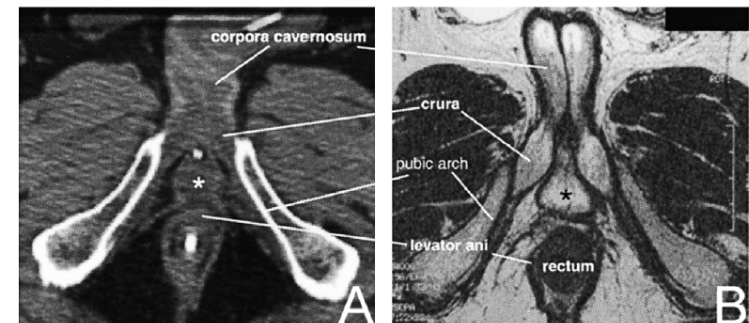
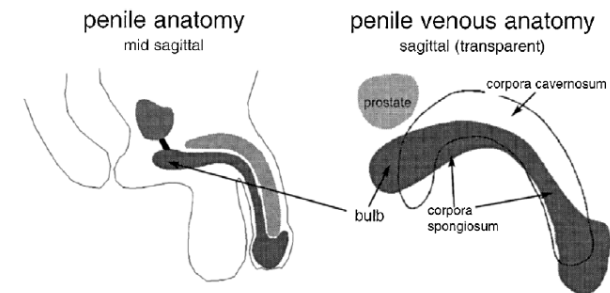
Physics Contribution

Contouring Variability of the Penile Bulb on CT Images: Quantitative Assessment Using a Generalized Concordance Index

Viviana Carillo, Ph.D.,* Cesare Cozzarini, M.D.,† Lucia Perna, Ph.D.,*
Mauro Calandra, M.Sc.,* Stefano Gianolini, Ph.D.,‡ Tiziana Rancati, Ph.D.,§
Antonello Enrico Spinelli, Ph.D.,* Vittorio Vavassori, M.D.,¶ Sergio Villa, M.D.,||
Riccardo Valdagni, M.D.,§,|| and Claudio Fiorino, Ph.D.*



Int J Radiation Oncol Biol Phys, Vol. 84, No. 3, pp. 841–846, 2012



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QUANTEC: ORGAN-SPECIFIC PAPER

Pelvis: Penile Bulb

RADIATION DOSE–VOLUME EFFECTS AND THE PENILE BULB

Table 1. Erectile dysfunction after external-beam radiotherapy and correlated parameters

First author, year (reference)	N	Assessment method*	Prescribed dose, treatment	OAR definition	Severe ED rate (%)	Correlated parameters	
						Dose–volume	Clinical
Fisch, 2001 (7)	21	Questionnaire [†]	65–72 Gy, 3D	Penile bulb	33 [‡]	D70 ≥70 Gy [§]	No other endpoints analyzed
Roach, 2004 (10)	158	Patient report, (RTOG)	68.4 Gy, 73.8 Gy, 3D	Penile bulb [¶]	41	Median penile bulb dose ≥52.5 Gy [¶]	No other endpoints analyzed
Wemick, 2004 (14)	29	Questionnaire [†]	66.6–79.2 Gy, 3D	Penile bulb [#]	NS	D30 ≥67 Gy [¶] D45 ≥63 Gy [¶] D60 ≥42 Gy [¶] D75 ≥20 Gy [¶]	Alcohol and smoking not significant, dose and volume significant
Selek, 2004 (11)	28	Questionnaire [†]	78 Gy, 3D	Penile bulb [#]	35.7% at 2 y	Mean dose to penile structure 38.2 Gy, no dose–volume effect was found [#]	Up to 68% may have had ED posttreatment? ED correlated with hypertension
Mangar, 2006 (8)	51	Questionnaire [†]	64 Gy, 74 Gy, 3D	Penile bulb, crura and cavernosum ^{**}	24	D15, D30, D50, D90 of penile bulb [¶]	Adjusted for age, bulb volume, hypertension, and previous pelvic surgery
Zelevsky, 2006 (15)	561	Patient report (NCI) ^{††}	81 Gy, IMRT	††	49	Not evaluated	Hormone therapy
Brown, 2007 (5)	32	Questionnaire [†]	NS, IMRT	Penile bulb	34	No relationship noted	Hypertension, pre-RT erectile function
Cahlon, 2008 (6)	478	Patient report (NCI) ^{††}	86.4 Gy, IMRT	††	30	Not evaluated	Age >70 y, diabetes, hormone therapy
van der Wielen, 2008 (13)	70	Questionnaire [†]	68 vs. 78 Gy	Penile bulb	36	No correlations between ED and dose–volume of crura, or the penile bulb [#]	Adjusted for diabetes and history of cardiovascular disease
Pinkawa, 2009 (9)	123	Questionnaire [†]	70.2–72 Gy, 3D	NS	73 ^{§§}	Not evaluated	Age, diabetes



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QUANTEC: ORGAN-SPECIFIC PAPER

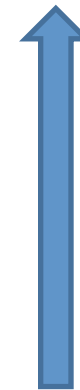
Pelvis: Penile Bulb

RADIATION DOSE–VOLUME EFFECTS AND THE PENILE BULB

MACK ROACH, III, M.D., FACR,* JIHO NAM, M.D.,[†] GIOVANNA GAGLIARDI, PH.D.,[‡]
ISSAM EL NAQA, PH.D.,[§] JOSEPH O. DEASY, PH.D.,[§] AND LAWRENCE B. MARKS, M.D.[†]

8. RECOMMENDED DOSE/VOLUME LIMITS

On the basis of the data available, it is prudent to keep the mean dose to 95% of the PB volume to <50 Gy. It may also be prudent to limit the D70 and D90 to 70 Gy and 50 Gy, respectively. It is acknowledged that the PB may not be the critical component of the erectile apparatus, but it seems to be a surrogate for yet to be determined structure(s) critical for erectile function for at least some techniques.



Future Directions

Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 3, pp. 752–759, 2008

CLINICAL INVESTIGATION

Prostate

***TGFB1* SINGLE NUCLEOTIDE POLYMORPHISMS ARE ASSOCIATED WITH ADVERSE QUALITY OF LIFE IN PROSTATE CANCER PATIENTS TREATED WITH RADIOTHERAPY**

CHRISTOPHER A. PETERS, M.D.,* RICHARD G. STOCK, M.D.,* JAMIE A. CESARETTI, M.D.,*
DAVID P. ATENCIO, PH.D.,* SHEILA PETERS, B.A.,* RYAN J. BURRI, M.D.,* NELSON N. STONE, M.D.,*†
HARRY OSTRER, M.D.,‡ AND BARRY S. ROSENSTEIN, PH.D.*§||¶

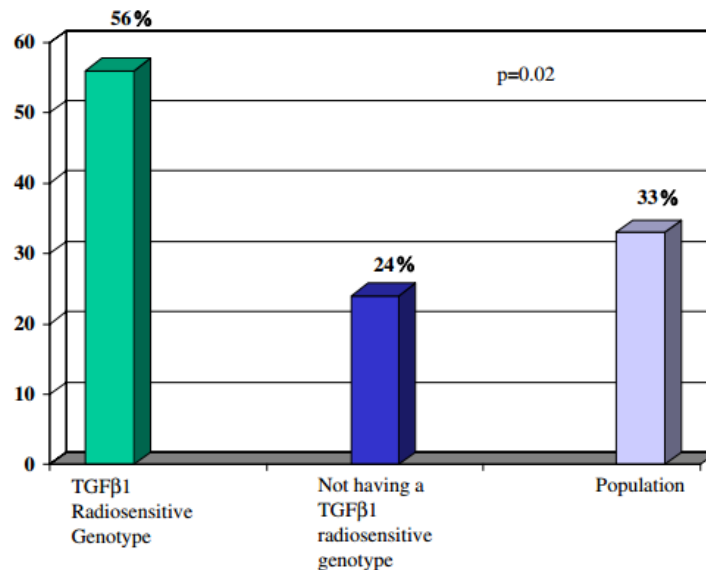


Fig. 1. Erectile dysfunction. Patients harboring single nucleotide polymorphisms in the –509TT, 869CC (T>C) (leu>pro) codon 10, or 915 (G>C) (arg>pro) codon 25 loci were found to have a 56% (9 of 16) prevalence of erectile dysfunction compared with 24% (11 of 45) for the remaining patients ($p = 0.02$). TGF β 1 = transforming growth factor β 1.



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Future Directions

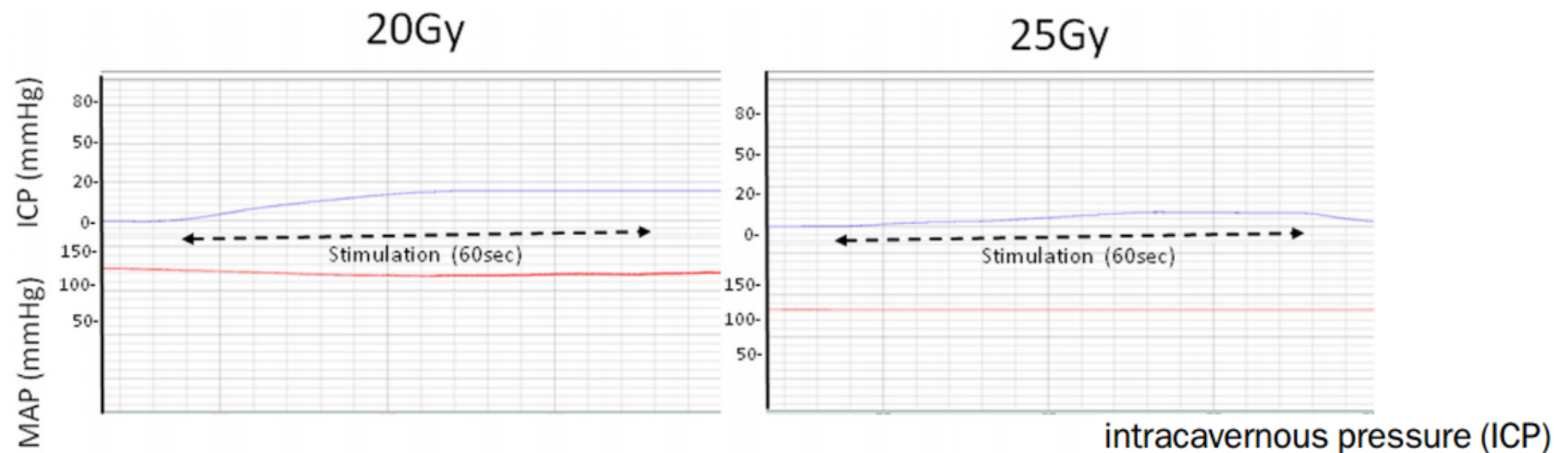
Basic and Translational Science

Pilot Study Evaluating a Rat Model of Radiation-induced Erectile Dysfunction Using an Image-guided Microirradiator



UROLOGY 85: 1214.e1–1214.e6, 2015. © 2015

Masaki Kimura, Andrew R. Zodda, Javed Mahmood, Shiva K. Das, Giao B. Nguyen, Isabel L. Jackson, and Zeljko Vujaskovic



Future Directions

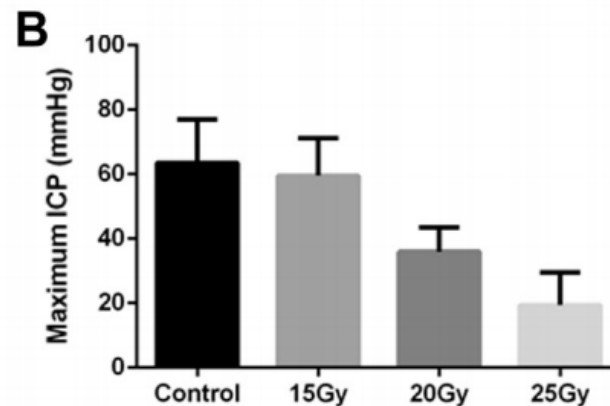
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UROLOGY 85: 1214.e1–1214.e6, 2015. © 2015

Masaki Kimura, Andrew R. Zodda, Javed Mahmood, Shiva K. Das, Giao B. Nguyen, Isabel L. Jackson, and Zeljko Vujaskovic



(B) ICP/mean arterial pressure ratio
intracavernous pressure (ICP)



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Conclusions

- Importance of sexual dysfunction for QoL
 - Baseline and post-RT evaluation
 - Evaluation of comorbidity
- The radiation induced ED is still debated and under evaluation
- The penile bulb spearing is recommended





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