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Sexual health and quality of life: Study on prostate cancer patients treated with modern 6MV X-ray radiation therapy

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***Abstract*---**This study aimed to compare the sexual quality of life through pre-defined parameters of prostate cancer (PCa) patients with pre-and-post- volumetric modulated arc radiation therapy (VMAT) and to examine their association with the radiation doses of the penile bulb (PB) and patient peculiarity. In this retrospective study, we analyzed medical record data of 100 patients who received definitive external radiation therapy (RT) and hormone therapy (HT) for prostate cancer (PCa) between June to December 2017. Sexual activities were analyzed by the patient-reported outcomes and clinician quality of life indices observed scale before and after treatment. The outcome of sexual activities was observed about patients' age, the volume of the prostate, the level of the testosterone, comorbidity, smoking habits, staging of the tumours, therapy technology, hormonal therapy (HT) and penile bulb (PB) radiation doses. 84 (84%) of all patients (n=100) after 2 years of radiation had a poor erectile grade, and 43 (75%) of previously potent (n=57) patients were impotent following treatment. However, sexual desire prevailed in 59 (76%) of patients who had desire before treatment. The statistical study found that the outcome of impotence post-radiation was associated with two variables; testosterone level (p=0.028) and mean radiation doses to the penile bulb (p=0.036). The sexual activity of prostate cancer (PCa) patients in various degrees, affect modern techniques. Reduce doses of radiation to the penile structures can help prevent sexual dysfunction (SD).

***Keywords*---**Prostate cancer, Quality of life, Radiation doses, Sexual health, volumetric modulated arc therapy.

Introduction

Over the past decade, significant reformation over irradiation methods and radiation doses has been made, resulting in better post-radiation outcomes and toxicity in prostate cancer (PCa). A sophisticated treatment planning system (TPS) permitted the implementation of volumetric modulated arc therapy (VMAT) and intensity-modulated radiation therapy (IMRT) that allows for an adequate radiation dose delivery with improved healthy tissue sparing. The earlier conformal radiation therapy methods were rendered obsolete by VMAT and IMRT. The medical accelerator designed with image-guided radiation therapy (IGRT) like implanted fiducial and cone-beam computed tomography (CBCT) has added even more accuracy and will potentially reduce toxicity. Several studies are ongoing for hypo-fractionated radiation therapy (RT) for PCa. Such routines will enhance clinical advantages, minimize toxicity, and have financial and logistical benefits. Since all these modern technologies have not yet proved therapeutic benefits in randomized clinical trials, they are just compared. Unfortunately, these technologies seem to induce post-treatment sexual dysfunction (SD), similar to traditional radiation therapy or even worse outcome [1].

The third International Sexual Medicine Consultation (ISMC) described sexual dysfunction (SD) as a persistent or recurring failure to sustain a proper penile erection for sexual performance [2]. Such a definition is explicitly applicable in a committed partner's presence and should thus be more appropriate for the general term sexual activity (sexual relations or masturbation)[3]. Psychological factors may play a significant role in sexual dysfunction (SD) after radiation therapy (RT).The researchers mentioned the potency or impotence word in most published studies without providing a clear, practical description [3]. The most realistic way of evaluating sexual function is to use a standard and numerous questionnaires in the literature have so far been used. For some instances, questions associated with sexual functioning were confined to a few issues or were combined into radiation toxicity or quality of life (QoL). The entire survey was not included in the articles with a few exceptions. “In the late 1990s, the international index of erectile function (IIEF) was established” [4], followed by a “shortened IIEF-5 questionnaire (also known as the Sexual Health Inventory for Men or SHIM)” [5].

Our objective was to evaluate the sexual function of patients who underwent modern radiotherapy like VMAT, IMRT with IGRT and to investigate the impact of PB radiation doses and patient characteristics on erectile dysfunction (ED).

1. Materials and methods.

1.1. Patient selection

Through our medical record database, we retrospectively included non-metastasis PCa patients treated with VMAT and IMRT definitive external beam radiation therapy (EBRT), between June to December, 2017. The inclusion criteria for selection were as follows; patients needed to have confirmed biopsy proven carcinoma prostate; patients performed all sexual function tests baseline and post

treatment indices defining sexual health were made available; patients had testosterone levels before treatment and at last follow-up (December 2019). Patients had periodic evaluation before the final assessment. Patients treated with androgen deprivation therapy (ADT) included before initiation of RT. Patients with prior Prostectomy and brachytherapy were excluded from the study. Patient characteristics are presented in Table 1.

Mean Age	63.21 ± 8.7
Age Group	
≤70	65
>70	35
Prostate Specific Antigen (PSA) Level (ng/mL)	38.7 (Mean)
Testosterone Level (ng/dL)	415.83
Gleason Score	
<7	18
7	9
>7	73
Androgen Deprivative Therapy (ADT)	
Yes	79
No	21
Prostate Volume (cc)	58.49 (Mean)
Smoking Habit	
Yes	73
No	27
Radiation Technique	
VMAT	68
IMRT/IGRT	22

Table 1. Physical characteristics of patient (n=100)

1.2. Treatment and assessment

Patients were categorized as per "European urology association (EUA) recommendations" [6] into three main categories: Low risk, intermediate medium risk and high risk. 21 Low-risk patients were treated with External RT alone, 37 medium risk patients treated with External RT + adjuvant HT (Short Course of 06 months), 42 high-risk patients treated with RT + HT (long course of 02 years) with LHRH agonists (Leuprolide + Bicalutamide).

All the patients were positioned in a supine position with a customized thermoplastic immobilization cast and computed tomography (CT) scan (Siemens Somatom Definition AS+, Siemens Healthcare, USA) images of 3 mm slice thickness were acquired. Bowel preparation was started three days prior to simulation and then continued throughout treatment. Bladder protocol was followed. A radiation oncologist contoured all the target structures such as Planning Target Volume (PTV), Clinical Target Volume (CTV), Gross Tumor Volume (GTV) and Organ at Risk structures (OARs) as per International Commission on Radiation Units and Measurements (ICRU) reports no. 50 and 62. All the patients who underwent RT planning were treated with VMAT and IMRT with IGRT techniques to a radiation dose of 76Gy (range 70-78Gy) for the prostate

and a 56Gy (range 54-56Gy) for the proximal seminal vesicles. Dose optimization was done using eclipse TPS version 13.6 (Varian Medical System, Palo alto, CA, USA). Dose-volume histograms (DVH) were used to assess the radiation dose in the rectum, bladder, femoral heads and PB to reduce toxicity. During the treatment, prostate localization was performed once a week by portal imaging or (CBCT) at the treatment time. Meanradiation doses of the PB and dosimetric sub-groups have been determined as V_{30Gy}, V_{50Gy}, V_{60Gy}, V_{70Gy} (volume of the PB receiving 70 Gy) and $D_{25\%}$, $D_{50\%}$, $D_{75\%}$, $D_{90\%}$ (90% dose to volume of the PB). In this study, medical accelerator True Beam STx (Varian Medical Systems, Palo Alto, CA, USA) was used.

1.3. Sexual health analysis

The measurement of sexual behavior was carried out using a patient-reported four-degree form [7]. Impotence was specified when the scores were 0 and 1 (Table 2).

Erectile Activity	**Score**
Normal erectile activity	3
Sub-optimal erections	2
Insufficient erections	1
Unable to have erection	0

Table 2. Erectile activity scoring questionnaire

"Sexual pleasure is measured by the patient clinical analysis of two questions chosen for patients with prostate cancer from the European Research and Care Organization on Cancer Quality of Life Questionnaire English Edition (ERCOC-QoL)" [8]. The nature of sexual desire was described as 3 or 4 from both questions (Table 3).

	Very much	Quite a bit	A little bit	Not at all
In the last 4 weeks, how involved were you in sex?	4	3	2	1
In the last 4 weeks, how often have you been sexually active?	4	3	2	1

Table 3. Sexual desire scoring questionnaire

The scale and questionnaire were applied before and after treatment for patients. The follow-up exams were required for patients every three months for the 1st year, then every six months. Age, prostate-specific antigen (PSA), staging, gleason score (GS), prostate volume, testosterone value, smoking habit, radiation techniques and other medical details have been recorded at the time of patient presentation in the hospital.

1.4. Statistical analysis

A quantitative analysis was carried out using IBM, version 20 of the SPSS software. Using the student t-test for quantitative variables and chi-2 testing for qualitative variables, univariate analysis was conducted. To prove a correlation between the factors Bravais-Pearson correlation coefficient was used. The statistical significance of the p-value was calculated below 0.05.

2. Results.

Our data surveyed 100 patients with an average age of 63.21±8.7. At the last follow-up(December 2019), all the patients were alive and free of illness. 43 (n=100) patients at presentation were sexually impotent. After the treatment, 43 (75%) of the previously potent 57 patients became sexually impotent (p<0.001). 22 patients out of 100 had no sexual desire prior to treatment. After the treatment, 19 (24%) of the 78 patients were found lost their sexual desire (p=0.0076). Erectile values were measured before and after treatment. Erectile values declined significantly (p<0.001). Overall, 86 out of 100 patients had reduced erectile levels, while 14 out of 100 had no change (Table 4).

	Before treatment	**After treatment**	**p-Value**
Normal erectile activity	39	7	<0.001
Sub-optimal erections	18	7	
Insufficient erections	29	48	
Unable to have erection	14	38	

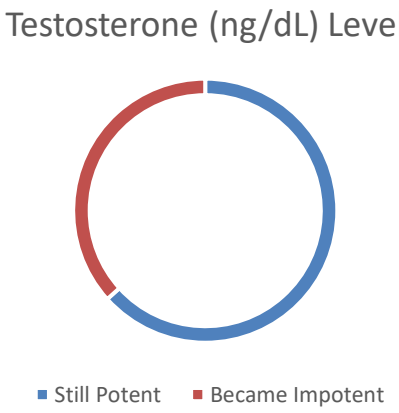
Table 4. Erectile scoring prior to and after treatment (n=100)

In terms of sexual potency, we graded patients into two categories: “potent” and “became impotent” after treatment. There were substantial variations between our median radiation dose to penile bulb groups and testosterone levels. A mean radiation dose of 28.97 Gy was given for patients who stayed potent, while the mean radiation dose for patients who became impotent was 49.60 Gy (p=0.036). Further assessment of the individual values showed that testosterone level, PB $D_{50\%}$, PB $D_{75\%}$ and PB $D_{90\%}$ doses were correlated with impotence level (p=0.028, 0.028, 0.018 and 0.016 respectively). There were no substantial differences between prostate volume and PSA levels (p=0.589 and p=0.897) (Table 5) (Graph 1 & 2).

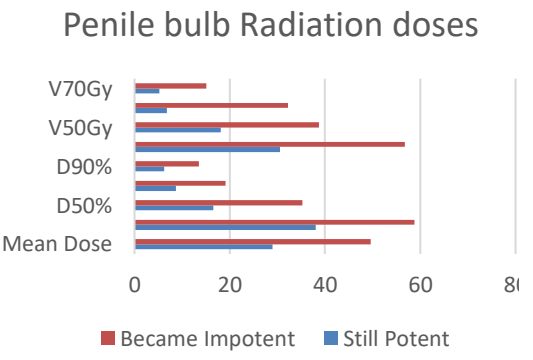
	Still potent (n=14)	Became impotent (n=43)	p-Value
Prostate volume (Mean Value)	60.20	74.80	0.589
PSA level (Mean Value)	9.23	8.37	0.897
Testosterone (ng/dL) (Mean Value)	483.24	241.94	0.028*
Mean Doses (Gy)	28.97	49.60	0.036*
$D_{25\%}$	38.03 (18-70)	58.80 (14.9-76.87)	0.121
$D_{50\%}$	16.50 (9-38)	35.26 (9.3-76.84)	0.028*
$D_{75\%}$	8.70 (7.8-14.8)	19.15 6.1-75.61)	0.018*

Penile bulb (Mean doses)	$D_{90\%}$	6.24 (5.8-9.3)	13.55 (5.8-70.2)	0.016*
	V_{30Gy}	30.50 (14-90)	56.78 (6.3-98)	0.126
	V_{50Gy}	18.15 (6.3-40.9)	38.75 (2-98)	0.078
	V_{60Gy}	6.81 (3.2-35.78)	32.20 (2-97.3)	0.121
	V_{70Gy}	5.20 (1.67-28.80)	15.05 (2-91.53)	0.251

Table 5. Characteristics associated with sexual activity after treatment (n=57)



Graph 1 – Testosterone Level



Graph 2 – Penile bulb radiation dose distribution

We observed that tumour staging, gleason score, smoking habit and hormone therapy had no substantial impact on potency. The rates of sexual dysfunction according to hormone therapy for 57 patients previously potent were 18/25 for hormone-naive therapy, 9/9 for short term and 16/23 for long term participants. We have also studied the same variables for patients who have lost their sexual desires and who have a sexual desire after treatment, but no substantial differentiation has been observed for our groups concerning the same variable.

Discussions

Our analysis had 100 patients with active prostate cancer, who received definite radiation treatment with or without hormone therapy. Most trials restrict those patients who were undergoing adjuvant hormone therapy. “The intention we included these patients were to determine the actual impact of EBRT and ADT on sexual activity, and because of some studies documented an insignificant influence of adjunct hormone therapy” [9]. A recent population oriented observational study which examined patient outcomes three years after treatment suggested that sexual activities in contrast to radiation therapy and active surveillance are worse with surgery. “The three-year potency preservation rate for prostectomy, radiation therapy, and intensive screening of patients with adequate erections prior to treatment was 43%, 53%, and 75%, respectively” [10]. “Two

prospective studies reported the rate of sexual dysfunction as 30-40% within 02 years following 3D-radiation therapy" [11, 12]. Several studies have suggested that IMRT/VMAT can be a better treatment choice because the adjacent structures receive lower doses of radiation [13]. In comparison, the erectile level of 64% of our patients has declined while IMRT/IGRT/VMAT is included.

There are many explanations for why our patients might have poorer sexual functioning than other trials with elevated impotence rates. First, 42%of patients underwent long term hormone treatment to help control their malignancy. New research, which involved 1,641 men treated for prostate cancer with initials of 358 ng / dL testosterone, showed that after 6–12 months of termination of ADT, the testosterone levels were 96 ng / dL and 273 ng / dL after two years. "The recovery rate was slightly shorter in patients of greater than 65 years of age who had a total of more than equal to 6 months ADT and a mean testosterone level of less than 400ng/dL" [14]. According to these results, the 1-year waiting time might not be enough for testosterone recovery in our sample group. Second, none of our patients used any pharmacological agent or potency aid during sexual function and impotence scaling. ED therapy will enhance the patient's sexual health. Third, according to the 2017 report of the male sexual health research group of the turkey society of andrology, the prevalence of ED is 68.8% among the Turkish population aged 60-69 years and 82.9% aged 70 years. They observed that age was the key indicator of ED, with a significant association of diabetes, asthma, atherosclerosis, dyslipidemia, lower urinary tract symptoms, educational status and months of income" [15]. However, a statistically significant effect of comorbidity and hormone therapy on sexual functioning could not be observed. Elevated ED concentrations and limited patients may obscure the substantial influence in these primary influences on sexual activity. Also, the mean age of our patients was 63.21, and certain comorbid subclinical conditions may exist. ED rates can, therefore, increase every year even without treatment.

The statistical evaluation found in our study that the mean radiation dose of PB and testosterone levels was significantly correlated with impotence development. Several reports evaluate the dose impact of RT on anatomical structures report conflicting findings. "There was no substantial association with the mean PB radiation dose observed in two major brachytherapy studies" [16,17]. "An analysis of 28 patients receiving 3D RT by Selek et al. showed no correlation between the occurrence of impotence and the radiation doses on PB and corpora cavernosa" [18]. Also, "Brown et al. [12] observed that post-treatment ED dose not contribute to the dose and volume of RT treatment in PB (p=0.38 and 0.76, respectively)". Even so, an analysis by "Wernicke et al. [19] that had a median following 35 months and evaluated erectile status via an EDFS (ED firmness score) revealed that the lower doses of radiation to a smaller volume of the PB had a higher conservation potency rate". They suggested that EBRT destroy the vascular and nerve system that directly or indirectly supports the cavernosa smooth muscles, resulting in impotence. A dose-escalation analysis of 158 patients by Roach et al. (RTOG 9406) has shown that ED development is correlated with the doses obtained from the penile system. Patients receiving an average PB dose of 52.5 Gy per 3D RT were confirmed to be at a higher risk of ED than those receiving a lower dose (p=0.039). They also stated that the age, doses or use of adjunct hormone therapy in the development of ED had little impact [9]. "A randomized

clinical study in 51 patients who underwent 3D RT and neoadjuvant hormonal therapy by Mangar et al. was conducted over the next three years and showed a substantial difference in mean dose in the PB (45.5, 48.0 and 59.2 respectively) in three groups (potent, reduced potency and impotent). They also observed that 83.3% of impotent patients received doses of PB D90 of the excess of 50Gy, although, for effective patients, this figure was just 29.4% for two years (p=0.006)" [20].

Our findings have shown a significant association between the mean PB dose and impotence development. We also observed that PB $D_{50\%}$, $D_{75\%}$ and $D_{90\%}$ were substantially correlated with impotence development when individual radiation doses were analyzed. In our study, we try to maintain the mean PB doses less than 50Gy. "Other than ED, sexual issues and symptoms after Radiation therapy for PCa include general ejaculation complications (lack of ejaculates, lower volume of ejaculations, pain during ejaculation, haemospermia), sexual frustration, reduced libido and sexual envy" [21]. We found that 78% of our patients had sexual desire prior to treatment and 54% persisted after therapy. In this situation, it is essential to recognize the risk and occurrence of sexual dysfunction following EBRT in the patient's quality of life (QoL).

Conclusions

Amid emerging technologies, ADT, or non-adjunct radiation therapy, impact men's sexual relationships with prostate cancer, and the penile bulb doses of radiation can be linked with erectile dysfunction.

References

[1] Goineau A, Campion L, d'Aillières B, Vié B, Ghesquière A, Béra G, Jaffres D, de Laroche G, Magné N, Artignan X, Chamois J, Bergerot P, Martin E, Créhange G, Deniaud-Alexandre E, Buthaud X, Belkacémi Y, Doré M, de Decker L and Supiot S 2018 Comprehensive Geriatric Assessment and quality of life after localized prostate cancer radiotherapy in elderly patients ed P Thumbikat *PLOS ONE***13** e0194173

[2] Montorsi F, Adaikan G, Becher E, Giuliano F, Khoury S, Lue T F, Sharlip I, Althof S E, Andersson K-E, Brock G, Broderick G, Burnett A, Buvat J, Dean J, Donatucci C, Eardley I, Fugl-Meyer K S, Goldstein I, Hackett G and Hatzichristou D 2010 Summary of the Recommendations on Sexual Dysfunctions in Men *The Journal of Sexual Medicine***7** 3572–88

[3] Incrocci L, Slob A K and Levendag P C 2002 Sexual (dys) function after radiotherapy for prostate cancer: a review *International Journal of Radiation Oncology, Biology, Physics***52** 681–93

[4] Rosen R C, Riley A, Wagner G, Osterloh I H, Kirkpatrick J and Mishra A 1997 The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction *Urology***49** 822–30

[5] Rosen R, Cappelleri J, Smith M, Lipsky J and Peña B 1999 Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction *International Journal of Impotence Research***11** 319–26

[6] Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch M G, De Santis M,

Fossati N, Gross T, Henry A M, Joniau S, Lam T B, Mason M D, Matveev V B, Moldovan P C, van den Bergh R C N, Van den Broeck T, van der Poel H G, van der Kwast T H, Rouvière O and Schoots I G 2017 EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent *European Urology***71** 618–29

[7] Zagar T M, Stock R G, Cesaretti J A and Stone N N 2007 Assessment of postbrachytherapy sexual function: a comparison of the IIEF-5 and the MSEFS *Brachytherapy***6** 26–33

[8] van Andel G, Bottomley A, Fosså S D, Efficace F, Coens C, Guerif S, Kynaston H, Gontero P, Thalmann G, Akdas A, D'Haese S and Aaronson N K 2008 An international field study of the EORTC QLQ-PR25: a questionnaire for assessing the health-related quality of life of patients with prostate cancer *European Journal of Cancer (Oxford, England: 1990)***44** 2418–24

[9] Roach M, Winter K, Michalski J M, Cox J D, Purdy J A, Bosch W, Lin X and Shipley W S 2004 Penile bulb dose and impotence after three-dimensional conformal radiotherapy for prostate cancer on RTOG 9406: findings from a prospective, multi-institutional, phase I/II dose-escalation study *International Journal of Radiation Oncology, Biology, Physics***60** 1351–6

[10] Barocas D A, Alvarez J, Resnick M J, Koyama T, Hoffman K E, Tyson M D, Conwill R, McCollum D, Cooperberg M R, Goodman M, Greenfield S, Hamilton A S, Hashibe M, Kaplan S H, Paddock L E, Stroup A M, Wu X-C and Penson D F 2017 Association Between Radiation Therapy, Surgery, or Observation for Localized Prostate Cancer and Patient-Reported Outcomes After 3 Years *JAMA***317** 1126

[11] Pinkawa M, Gagel B, Piroth M D, Fischedick K, Asadpour B, Kehl M, Klotz J and Eble M J 2009 Erectile dysfunction after external beam radiotherapy for prostate cancer *European Urology***55** 227–34

[12] van der Wielen G J, van Putten W L J and Incrocci L 2007 Sexual function after three-dimensional conformal radiotherapy for prostate cancer: results from a dose-escalation trial *International Journal of Radiation Oncology, Biology, Physics***68** 479–84

[13] Brown M W, Brooks J P, Albert P S and Poggi M M 2006 An analysis of erectile function after intensity modulated radiation therapy for localized prostate carcinoma *Prostate Cancer and Prostatic Diseases***10** 189–93

[14] Miranda E P, Nelson C J, Schofield E A and Mulhall J P 2017 MP91-10 TESTOSTERONE RECOVERY PROFILES AFTER CESSATION OF ANDROGEN DEPRIVATION THERAPY (ADT) *Journal of Urology***197**

[15] Çayan S, Kendirci M, Yaman Ö, Aşçı R, Orhan İ, Usta M F, Ekmekçioğlu O and Kadıoğlu A 2017 Prevalence of erectile dysfunction in men over 40 years of age in Turkey: Results from the Turkish Society of Andrology Male Sexual Health Study Group *Turkish Journal of Urology***43** 122–9

[16] Macdonald A G, Keyes M, Kruk A, Duncan G, Moravan V and Morris W J 2005 Predictive factors for erectile dysfunction in men with prostate cancer after brachytherapy: is dose to the penile bulb important? *International Journal of Radiation Oncology, Biology, Physics***63** 155–63

[17] Merrick G S, Butler W M, Wallner K E, Galbreath R W, Anderson R L, Kurko B S, Lief J H and Allen Z A 2005 Erectile function after prostate brachytherapy *International Journal of Radiation Oncology, Biology, Physics***62** 437–47

[18] Selek U, Cheung R, Lii M, Allen P, Steadham R E, Vantreese T R, Little D J, Rosen I I and Kuban D 2004 Erectile dysfunction and radiation dose to penile base structures: a lack of correlation *International Journal of Radiation Oncology, Biology, Physics***59** 1039–46

[19] Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2022). Post-pandemic health and its sustainability: Educational situation. International Journal of Health Sciences, 6(1), i-v. https://doi.org/10.53730/ijhs.v6n1.5949

[20] Wernicke A G, Valicenti R, Dieva K, Houser C and Pequignot E 2004 Radiation dose delivered to the proximal penis as a predictor of the risk of erectile dysfunction after three-dimensional conformal radiotherapy for localized prostate cancer *International Journal of Radiation Oncology, Biology, Physics***60** 1357–63

[21] Mangar S A, Sydes M R, Tucker H L, Coffey J, Sohaib S A, Gianolini S, Webb S, Khoo V S, MRC RT01 Trial Management Group and Dearnaley D P 2006 Evaluating the relationship between erectile dysfunction and dose received by the penile bulb: using data from a randomised controlled trial of conformal radiotherapy in prostate cancer (MRC RT01, ISRCTN47772397) *Radiotherapy and Oncology: Journal of the European Society for Therapeutic Radiology and Oncology***80** 355–62

[22] Incrocci L 2011 Is there a sexual life after treatment of prostate cancer? *Journal of Men's Health***8** S1–3