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Erectile dysfunction after prostate three-dimensional conformal radiation therapy

Correlation with the dose to the penile bulb

Prostate cancer is the most common nonskin cancer and the second most common cause of cancer death in men [1]. For the majority of men with incident prostate cancer (approximately 85%), the disease is diagnosed as localized (T1–2). When the disease is organ confined the definitive treatment options commonly include: radical prostatectomy, external beam radiation therapy (EBRT), and brachytherapy.

Evidence suggests that, among these treatment modalities, brachytherapy is associated with the lowest risk of erectile dysfunction (ED). In a meta-analysis of patients treated for localized prostate cancer, the predicted probability of maintaining erectile function after 1 year was 76% with brachytherapy, 55% with EBRT, and 34% with nerve-sparing radical prostatectomy [2]. However, this improved rate of potency preservation may not persist with longer follow-up [3].

Work from the Comprehensive Cancer Center of San Francisco, California, also based on animal studies [4], shows that damage to nerves in the penile bulb (PB) is involved in radiation-induced impotence. Other reports confirmed an association between the technique used to deliver radiotherapy and radiation-induced impotence correlated with the bulb dose.

Pinkawa et al. [5] have evaluated the treatment-related morbidity after intensity-modulated (IMRT) and image-guided (IGRT) radiotherapy for patients with prostate cancer. The authors concluded that the combination of dose escalation with technological advances (IMRT and IGRT) is not associated with an increase in ED.

Few studies have evaluated sexual function after three-dimensional conformal radiation therapy (3D-CRT) as compared to pretreatment baseline values [6], but complete pre- and post-3D-CRT sexual function data are critical for this assessment.

The purpose of this study was to determine whether the radiation dose delivered to the PB during definitive 3D-CRT for prostate cancer correlates with the development of impotence.

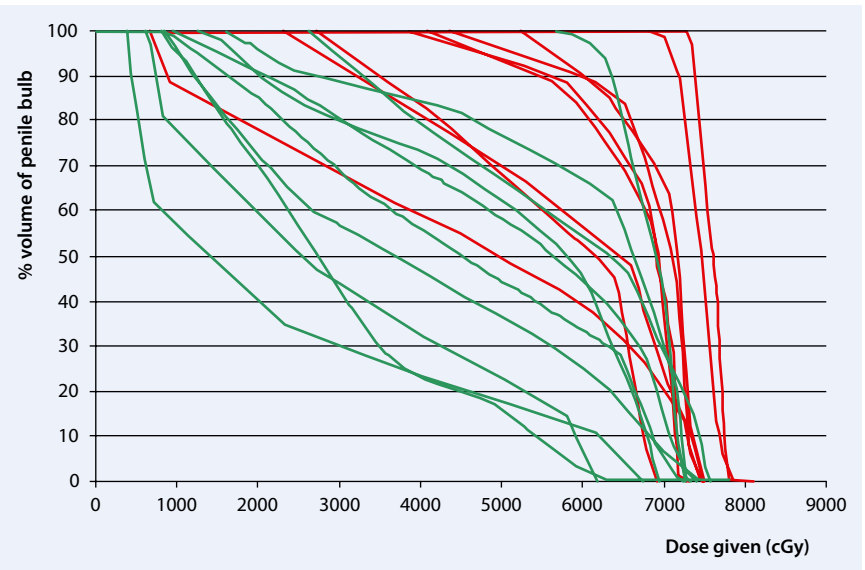

Fig. 1 ▲ Comparison of the dose–volume histograms of the penile bulb in potent (*green*) and impotent (*red*) patients

Tab. 1 The 5-item International Index Erectile Function score is the sum of questions 1–5. The lowest score is 5 and the highest score 25

	Score				
Over the past 6 months	**1**	**2**	**3**	**4**	**5**
How do you rate your confidence that you could get and keep an erection?	Very low	Low	Moderate	High	Very high
When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	Almost never or never	Much less than half the time	About half the time	Much more than half the time	Almost always Or always
During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	Almost never or never	Much less than half the time	About half the time	Much more than half the time	Almost always or always
During sexual intercourse how difficult was it to maintain your erection to the completion of intercourse?	Extremely difficult	Very difficult	Difficult	Slightly difficult	Not difficult
When you attempted sexual intercourse, how often was it satisfactory for you?	Almost never or never	Much less than half the time	About half The time	Much more than half the time	Almost always or always

Tab. 2 Level of sexual function according to the IIEF–5

Normal	Range from 25 to 22
Erectile dysfunction mild	Range from 21 to 17
Erectile dysfunction mild to moderate	Range from 16 to 12
Erectile dysfunction moderate	Range from 11 to 8
Erectile dysfunction severe	Range from 7 to 5

Tab. 3 Patients' characteristics

Characteristics	**Value**
Age (years)	
Mean SD	74.2±5.2
Median	74
Range	59–80
Vascular disease	4
Diabetes	0
Stage	
T1	10 (52.6)
T2	6 (31.6)
T3	3 (15.8)
PSA	
<10 ng/ml	9 (47.4)
>10 ng/ml <20 ng/ml	2 (10.5)
>20 ng/ml	8 (42.1)
Gleason score	
6	4 (21)
7	10 (52.6)
8–10	5 (26.4)
Hormonal Therapy	0
Phosphodiesterase type 5 inhibitor	0

Data in parentheses are percentages

Patients and methods

The retrospective study was approved by the ethics board, and all patients provided written informed consent. The inclusion criteria for the study were that all patients: (a) had not received neoadjuvant hormonal therapy (HT) and phosphodiesterase type 5 inhibitor, (b) had undergone a well-known pretreatment sexual evaluation, and (c) had available follow-up information.

Between September 2006 and October 2007, we enrolled 37 patients treated with 3D-CRT for clinically localized prostate cancer. All patients had completed 271 self-administered 5-item International Index Erectile Function (IIEF-5) questionnaires. From this group we considered 19 patients and we excluded 18 patients who received neoadjuvant hormonal therapy (HT). The IIEF-5 questionnaire we used is a sensitive, specific, and validated instrument for estimating multidimensional sexual function (**Tab. 1**). According to this survey, we divided patients into groups based on the levels of sexual function as indicated in **Tab. 2**.

All patients in the study did not have metabolic comorbidity: Diabetes mellitus, cholesterol, and atherosclerosis are cofactors for the risk of ED.

All patients received 3D-CRT as primary treatment with a median dose of 74.1 Gy (range 72–76 Gy). Patients were placed in the supine position and a urethrogram was obtained to assist in defining the apex of the prostate. We performed the simulation protocol using 5-mm axial computed tomography (CT) slices, with an empty rectum and full bladder. Slices were obtained to define the clinical tumor volume (CTV), the planning tumor volume (PTV), the body anatomy, the rectum, and the bladder.

The CTV volume was definite by the anatomical structure, the prostate, or the prostate and seminal vesicles; a uniform expansion of 1.0 and 0.8 cm versus the rectum was used to define the PTV volume.

For patients in the low-risk group, a dose of 72 Gy was delivered in a single-phase treatment covering the prostate and the base of the seminal vesicles with a 0.8- to 1.0-cm uniform margin. For patients in the high-risk group, a dose of 76 Gy was delivered in a two-phase treatment: first, the prostate and the whole volume of the seminal vesicles, with a 0.8- to 1.0-cm uniform margin, were irradiated at 56 Gy, followed by a boost of 20 Gy delivered only to the prostate gland. The dose was prescribed to the ICRU point, with the constraint of $D_{100\%}$ ≥95% of the prescribed dose. The definition and delineation of the PB and CTV were analyzed by the same physician (A.M.) so as to obtain uniformity of delineation.

The treatment plan was approved by the physician on the basis of the dose received by the target volume and of the dose–volume constraints for the rectum and bladder (V50 Gy <58%, V60 Gy <43%, and V70 Gy <25% for rectum volume, and V50 Gy <55%, V60 Gy <40%, and V70 Gy <25% for bladder volume).

The anatomy and imaging characteristics of the PB have previously been elegantly described and illustrated by Wallner et al. [7]. In our patient cohort the dose to the PB was calculated by contouring the structure and generating a dose–volume histogram (DVH) from the 3D-

CRT plan, which was approved by the physician and used to treat the patient. From each DVH, we obtained the values of $D_{30\%}$, $D_{50\%}$, $D_{60\%}$, $D_{70\%}$, $D_{80\%}$, $D_{90\%}$, and the mean doses delivered to the volume of the PB.

To estimate the risk of ED as a function of morphological and dosimetric parameters, an unconditional logistic regression model was applied and the odds ratio (OR) and 95% confidence interval (95% CI) were calculated.

The multivariate models were developed including the variables mean dose (D_{mean}). Then the mean dose was replaced consecutively by D_{30}, by D_{50}, by D_{60}, by D_{70}, by D_{80}, and by D_{90} and the baseline score of the questionnaire IIFE-5. The model included the overlap volume between the PTV and the PB (OVB) with the baseline IIEF-5 score. Both the absolute (OVBcc) and percentage (OVB%) volume were estimated.

Finally, to evaluate the dose–effect on ED we used a logistic regression model where the variable D_{mean} was dichotomized at different cut-off values.

Results

We considered 19 prostate cancer patients treated at our department between October 2006 and October 2007. The patients had not received HT, they had undergone a well-known pretreatment sexual evaluation, and they had follow-up information available. The average age at the time of radiotherapy was 59–80 years (median: 74 years). The patients presented with varied disease features, with one third having at least two higher risk factors. Three patients (15.8%) had stage T3 disease, 8 patients (42.1%) had pretreatment prostate-specific antigen values greater than 20 ng/ml, and 5 patients (26.3%) had Gleason scores between 8 and 10. The patients' characteristics at baseline are listed in **Tab. 3**.

All patients were self-reported to be potent before treatment. They were potent to different degrees: 11 (58%) were at a normal level and 8 (42%) were affected with mild ED.

All patients reported change in potency after radiation. Eight patients (42%) remained potent but showed a decrease

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Erectile dysfunction after prostate three-dimensional conformal radiation therapy. Correlation with the dose to the penile bulb

Abstract

Purpose. Erectile dysfunction is associated with all the common treatment options for prostate cancer. The aim of this research was to evaluate the relationship between erectile function and radiation dose to the penile bulb (PB) and other proximal penile structures in men receiving conformal radiotherapy (CRT) without hormonal therapy (HT) for prostate cancer, whose sexual function was known before treatment.

Patients and methods. The study included 19 patients treated with 3D-CRT for localized prostate cancer at our department, who were self-reported to be potent before treatment, had not received HT, and had complete follow-up data available. Our evaluation was based on the International Index of Erectile Function (IIEF-5). Dose–volume histograms (DVHs) were used to evaluate the dose to the PB. Statistical analysis was performed with an unconditional logistic regression model.

Results. All patients reported change in potency after radiation. Eight patients (42%) remained potent but showed a decrease of 1 or 2 levels of potency, as defined by the IIEF-5 questionnaire (reduced potency group), while 11 patients (58%) reported a change of higher levels and revealed a severe erectile dysfunction after 2 years (impotence group). Multivariate analysis of morphological and dosimetric variables yielded significance for the mean dose (p=0.05 with an odds ratio of 1.14 and 95% CI 1–1.30). Patients receiving a mean dose of less than 50 Gy to the PB appear to have a much greater likelihood of maintaining potency.

Conclusion. Our data suggest a possible existence of a dose–volume correlation between the dose applied to the PB and radiation-induced impotence.

Keywords

Prostate · Prostate cancer · Radiotherapy · Sexual dysfunction · Penile bulb

Erektile Dysfunktion nach dreidimensionaler konformaler Radiotherapie der Prostata. Korrelation mit der Dosis am Bulbus penis

Zusammenfassung

Ziel. Die erektile Dysfunktion ist mit allen üblichen Behandlungsoptionen des Prostatakarzinoms assoziiert. Ziel dieser Forschung ist die Analyse der Beziehung zwischen erektiler Funktion und Strahlendosis am Bulbus penis (PB) und anderen proximalen Penisstrukturen bei Männern mit konformaler Radiotherapie (CRT) wegen eines Prostatakarzinoms, aber ohne Hormontherapie (HT), deren sexuelle Funktion vor der Behandlung bekannt war.

Patienten und Methoden. Untersucht wurden 19 Patienten, die wegen eines lokalisierten Prostatakarzinoms mit 3-D-CRT in unserer Klinik behandelt wurden, sich vor der Behandlung als potent bezeichneten, keine HT bekommen hatten und über ein komplettes Follow-up verfügten. Unsere Analyse stützte sich auf den International Index of Erectile Function (IIEF-5). Dosis-Volumen-Histogramme (DVH) wurden verwendet, um die Dosis am PB zu bewerten. Die statistische Analyse wurde mit einem unbedingten logistischen Regressionsmodell durchgeführt.

Ergebnisse. Alle Patienten berichteten von einer Änderung der Potenz nach der Bestrahlung. Potent blieben 8 Patienten (42%), sie zeigten aber eine Abnahme der Potenz um 1 oder 2 Stufen, wie im IIEF-5-Fragebogen definiert (Gruppe mit reduzierter Potenz), während 11 Patienten (58%) von einer Änderung höheren Grades berichteten und nach 2 Jahren eine schwerwiegende erektile Dysfunktion aufwiesen (Gruppe mit Impotenz). In der multivariaten Analyse morphologischer und dosimetrischer Variablen ergab sich Signifikanz für die mittlere Dosis (p=0,05 bei Odds Ratio von 1,14 und 95%-Konfidenzintervall von 1–1,30). Bei Patienten, die eine mittlere Dosis unter 50 Gy am PB erhalten, besteht anscheinend eine deutlich größere Wahrscheinlichkeit des Potenzerhalts.

Schlussfolgerung. Unsere Daten weisen auf das mögliche Bestehen einer Dosis-Volumen-Korrelation zwischen der am PB verabreichten Dosis und strahleninduzierter Impotenz hin.

Schlüsselwörter

Prostata · Prostatakarzinom · Radiotherapie · Sexuelle Dysfunktion · Bulbus penis

Tab. 4 Relative probability of ED as a function of dosimetric and morphological parameters

Variables	Odds ratio	95% CI	p	Odds ratio (without IIEF)	95% CI (without IIEF)	p (without IIEF)
D_{mean}	1.14	1–1.30	0.06	1.14	1.01–1.28	0.03
IIEF	0.83	0.66–1.05	0.12			
D_{50}	1.13	0.98–1.3	0.09	1.13	1–1.28	0.06
IIEF	0.83	0.66–1.04	0.01			
D_{60}	1.02	0.96–1.09	0.53	0.99	0.94–1.03	0.61
IIEF	0.78	0.61–1	0.05			
D_{70}	1.02	0.96–1.09	0.51	0.99	0.95–1.03	0.56
IIEF	0.78	0.60–1	0.05			
D_{80}	1.03	0.96–1.10	0.42	0.99	0.95–1.03	0.57
IIEF	0.76	0.58–1	0.05			
D_{90}	1.08	1.01–1.16	0.03	1.07	1.01–1.14	0.02
IIEF	0.78	0.6–1.02	0.07			
OVBcc	0.43	0.05–3.69	0.44	0.54	0.16–1.81	0.32
OVB%	1.13	0.96–1.33	0.15	1.07	1.01–1.13	0.02
IIEF	0.67	0.38–1.19	0.18			

Tab. 5 Dose–effect relationship between ED and D_{mean}

Variables mean (D_{mean})	Odds ratio	95% CI	p
D_{mean}	0.054	0.004–0.64	0.02
D_{mean}-45Gy	0.13	0.011–1.41	0.09
D_{mean}-49Gy	0.13	0.011–1.41	0.09
D_{mean}-50Gy	0.08	0.007–0.95	0.04
D_{mean}-51	0.05	0.004–0.64	0.02

of 1 or 2 levels of potency, as defined by the IIEF-5 questionnaire (reduced potency group), while 11 patients (58%) reported a change of higher levels and revealed severe ED after 2 years (impotence group).

The clinical stage was fairly well balanced between the two groups (reduced potency and impotence). Although men who became impotent were a little older (median age 76 years; range 69–80 years) than those who reported reduced potency (median age 73 years; range 59–78 years), no association was seen between age and retention of potency after radiation treatment (p=0.11).

To estimate the risk (odds ratio) of ED, an unconditional multivariate logistic regression model was used as a function of morphological and dosimetric parameters. The significance level for the analysis was set to p=0.05. The results are reported in **Tab. 4**.

We found significance only for the D_{mean} (p=0.05) with an odds ratio of 1.14 and 95% CI 1–1.30, indicating an additional risk of developing ED of 14% for every increase of 1 Gy of the D_{mean}.

As can be seen, the dosimetric parameters of D_{30}–D_{50}–D_{60}–D_{70}–D_{80}–D_{90} are not statistically significant for ED, but become significant with the baseline score of the IIFE-5 (**Tab. 4**).

Finally, to determine a dose–effect relationship in ED, the variable D_{mean} was dichotomized at different cut-off values. The results are presented in **Tab. 5**. Statistical significance is noted for a mean dose of 50 Gy (p=0.04) with an odds ratio of 0.08 and 95% CI 0.007–0.95.

The D_{mean} delivered to the PB can be used to estimate a dose–volume constraint by comparing the relative proportion of patients in each potency group that exceed a specific dose cut-off point.

A threshold value of 50 Gy to the PB can be used to discriminate between the reduced potency and the impotence groups. **Fig. 1** shows the results of the comparison of the DVHs of the PB in the potent and impotent patients.

Discussion

The survival rates after radiotherapy and radical surgery as the definitive treatment for prostate cancer appear to be comparable. Therefore, the selection of treatment options is often based on the expected side effects, such as impotence and incontinence.

To our knowledge, only three published papers have reported specifically on the etiology of ED after estrogen replacement therapy [8, 9, 10].

In our study, the D_{mean} was found to be more predictive than the D_{50} normally quoted, because differences only became apparent as the dose accumulated with the increasing volume irradiated. Nevertheless, the difference between these two dose–volume parameters is small and clinically negligible. Most studies suggest a median dose (D_{50}) of 50 Gy or more as a cut-off point, over which there is a higher chance of developing potency [11, 12, 13].

Our results illustrate that impotent patients received a D_{mean} of 50 Gy or more compared to those who maintained potency above this dose level.

In 2006, Mangar et al. [14] from the Medical Research Council (MRC), according to results of the Radiation Therapy Oncology Group Trial 9406 (RTOG 9406), concluded that as the PB dose increases the change in ED becomes greater. Their results show that a significant proportion of impotent patients received a D_{90} of 50 Gy or more compared to those who maintained potency above this dose level (83.3% vs. 29.4%, p=0.006) [14].

By contrast, other authors have questioned the existence of a significant correlation between the dose to the PB and risk of ED [11, 12, 15]. It is possible that owing to the lack of feedback, in many of the studies analyzed, statistically significant correlations between the dose delivered to the structures mentioned so far and the risk of ED are a result of, at least in part, the retrospective nature and small number of these series as well as the reduced quality of the dosimetric data (DVH) for these structures [16].

Other factors in addition to the dose may have an impact on the recovery of potency, including social factors, increased age, and particularly psychological status. Another equally important reason for considering outlining the PB routinely as an avoidance structure is

that it helps to identify at least where the prostatic apex lies. This location should help with better delineation of the high-dose area and not compromise the dose to the target volume.

Additional studies are warranted to evaluate which dose–volume relationships are most important for preservation of potency. Moreover, the maximal dose to the prostate did not impact potency outcome. Likewise, in an analysis of data from the RTOG 9406, Roach et al. [17] noted no relationship between the total dose and potency.

Although the number of patients in our study is small and the range of doses to the PB is broad and overlapping, we believe that these results warrant the use of pelvic magnetic resonance imaging (MRI) in addition to CT to improve the localization of the prostate apex and of the PB and consequently result in a reduction of the dose to the PB, independently of the delivery technique (IMRT—helical tomotherapy) [18].

By contrast, other authors [5, 19] have reported on the use of IMRT to administer a reduced dose to critical structures such as the rectum and PB. These techniques have the potential to improve the preservation of potency further by minimizing the bulb dose.

Moreover, the incorporation of adaptive image-guided radiotherapy (IGRT) reduces the risk of a geometric miss and results in excellent biochemical control and low toxicity to organs at risk [20].

Since 2009, patients with localized prostate cancer have been treated in our department with IGRT with daily correction of the target position based on kilovoltage imaging of implanted prostatic fiducial markers and the definition and delineation of PB and CTV by 3T-MRI images

Sildenafil improves the erectile function in 71% of patients with radiation-induced ED [21]. It is likely that sparing the PB during radiotherapy will improve the efficacy of such medical therapies for impotence.

Larger studies with longer follow-up are required to definitively prove our working hypothesis. The preliminary data for patients treated in the RTOG Trial 9406 also revealed a correlation between the dose to the PB and an increased risk of impotence beyond 2 years [13].

Conclusion

Our data suggest that a dose–volume relationship may exist between the dose to the PB and radiation-induced impotence. There was a significant decrease in self-reported scores from baseline at 6 months after EBRT compared to degradation from 6 to 24 months. Moreover, in agreement with other investigators, there was a correlation between the self-reported score after radiotherapy and the self-reported score before the initiation of treatment [22, 23]. This information can help patients to have realistic expectations of the treatment outcomes.

Since a D_{mean} of 50 Gy or more is associated with a significant risk of ED, we propose a threshold dose for preservation of potency between 45 and 40 Gy. Longer follow-up is needed to validate our results, as potency appears to decrease with time after radiotherapy [10]. We hope to incorporate the findings from this study into the development of future studies looking at refining the dose constraints for the PB and associated proximal penile tissue for high-dose IMRT with gold fiducial markers.

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Conflict of interest. On behalf of all authors, the corresponding author states that there are no conflicts of interest.

References

1. Merrick GS, Butler WM, Lief JH, Dorsey AT (2001) Is brachytherapy comparable with radical prostatectomy and external-beam radiation for clinically localized prostate cancer? Tech Urol 7:12–19
2. Robinson JW, Moritz S, Fung T (2002) Meta-analysis of rates of erectile function after treatment of localized prostate carcinoma. Int J Radiat Oncol Biol Phys 54:1063–1068
3. Merrick GS, Wallner KE, Butler WM (2003) Management of sexual dysfunction after prostate brachytherapy. Oncology (Wilston Park) 17:52–62
4. Carrier S, Hricak H, Lee SS et al (1995) Radiation-induced decrease in nitric oxide synthase-containing nerves in the rat penis. Radiology 195:95–99
5. Pinkawa M, Piroth MD, Djukic V et al (2011) Combination of dose escalation with technological advances (intensity-modulated and image guided radiotherapy) is not associated with increased morbidity for patients with prostate cancer. Strahlenther Onkol 187:479–484
6. Turner SL, Adams K, Bull CA, Berry MP (1999) Sexual function after radical radiation therapy for prostate cancer: a prospective evaluation. Urology 54:124–129
7. Wallner KE, Merrick GS, Benson ML et al (2002) Penile bulb imaging. Int J Radiat Oncol Biol Phys 53(4):928–933
8. Goldstein I, Feldman MI, Deckers PJ et al (1984) Radiation-associated impotence. A clinical study of its mechanism. JAMA 251:903–910
9. Mittal B (1985) A study of penile circulation before and after radiation in patients with prostate cancer and its effect on impotence. Int J Radiat Oncol Biol Phys 11:1121–1125
10. Zelefsky MJ, Eid JF (1998) Elucidating the etiology of erectile dysfunction after definitive therapy for prostatic cancer. Int J Radiat Oncol Biol Phys 40:129–133
11. Fisch BM, Pickett B, Weinberg V, Roach M (2001) Dose of radiation received by the bulb of the penis correlates with risk of impotence after three-dimensional conformal radiotherapy for prostate cancer. Urology 57:955–959
12. Merrick GS, Wallner K, Butler WM et al (2001) A comparison of radiation dose to the bulb of the penis in men with and without prostate brachytherapy-induced erectile dysfunction. Int J Radiat Oncol Biol Phys 50:597–604
13. Roach M, Winter K, Michalski JM et al (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. Int J Radiat Oncol Biol Phys 60:1351–1356
14. Mangar SA, Sydes MR, Tucker HL et al (2006) Evaluating the relationship between erectile dysfunction and dose received by the penile bulb: using data from a randomised controller trial of conformal radiotherapy in prostate cancer (MRC RT01, ISRCTN47772397). Rad oncol 80:355–362
15. Kiteley RA, Lee WR, deGuzman AF et al (1908) Radiation dose to the neurovascular bundles or penile bulb does not predict erectile dysfunction after prostate brachytherapy. Brachytherapy 1:90–94
16. Nelson CJ, Choi JM, Mulhall JP et al (2007) Determinants of sexual satisfaction in men with prostate cancer. J Sex Med 4:1422–1427
17. Roach M, Pickett B, Holland J et al (1993) The role of the urethrogram during simulation for localized prostate cancer. Int J Radiat Oncol Biol Phys 25:299–307

18. Perna L, Fiorino C, Cozzarini C et al (2009) Sparing the penile bulb in the radical irradiation of clinically localised prostate carcinoma: a comparison between MRI and CT prostatic apex definition in 3DCRT, Linac-IMRT and Helical Tomotherapy". Radiat Oncol 93:57–63
19. Geier M, Astner ST, Duma MN et al (2012) Dose-escalated simultaneous integrated-boost treatment of prostate cancer patients via helical tomotherapy. Strahlenther Onkol 188:1–7
20. Park SS, Di Yan, McGrath S, Dilworth JT et al (2012) Adaptive image-guided radiotherapy (IGRT) eliminates the risk of rectal distension in prostate cancer treatment planning: clinical evidence. Int J Radiat Oncol Biol Phys 83:947–952
21. Kedia S, Zippe CD, Agarwal A et al (1999) Treatment of erectile dysfunction with sildenafil citrate (Viagra) after radiation therapy for prostate cancer. Urology 54:308–312
22. Di Blasio CJ, Malcolm JB, Derweesh IH et al (2008) Patterns of sexual and erectile dysfunction and response to treatment in patients receiving androgen deprivation therapy for prostate cancer. BJU Int 102:39–43
23. Wielen GJ van der, Putten WL van, Incrocci L et al (2007) Sexual function after three-dimensional conformal radiotherapy for prostate cancer: results from a dose-escalation trial. Int J Radiat Oncol Biol Phys 68:479–484