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Prostate brachytherapy

An analysis of the relation between physical characteristics of prostate I-125 seed implants and lower urinary tract symptoms: Bladder hotspot dose and prostate size are significant predictors

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Abstract

***Purpose*: Lower urinary tract symptoms are frequently observed after I-125 seed implantation of the prostate. More knowledge about causes and predictors is necessary to be able to develop less toxic implantation techniques. The aim of this study was to identify implantation related factors that contribute to post-implant urinary morbidity.**

***Materials and methods*: Analysed was a group of 72 patients that filled in a symptom score questionnaire before, 3 months and 6 months after implantation as well as a group of 15 patients that suffered from acute urinary retention. Several dose—volume parameters of prostate, urethra and bladder wall were determined based on a post-implant TRUS-CT scan.**

***Results*: The dose to a 1 cm^3 hotspot in the bladder wall (D1cc-bl) as well as the prostate volume were independently correlated with urinary morbidity symptom scores at 3 months ($p = 0.006$ and $p = 0.005$, respectively) and at 6 months ($p = 0.001$ and $p = 0.015$, respectively) after implantation. The number of implanted seeds and the D1cc-bl were significant discriminators ($p < 0.001$ and $p = 0.015$, respectively) for either mild or severe early urinary morbidity.**

***Conclusion*: Bladder hotspot dose appears to be an important dosimetric predictor for urinary morbidity both at 3 months and at 6 months after implantation. Other predictors are prostate volume, or equivalently, the number of implanted seeds.**

Keywords: Prostate brachytherapy; Urinary morbidity; Bladder dose; Prostate volume

Implantation of the prostate with I-125 seeds is a well-established treatment for early-stage prostate cancer. In general this brachytherapy treatment is relatively well tolerated [1—5]. Nevertheless, most patients experience lower urinary tract symptoms (LUTS) to some degree after implantation. The nature of the complaints is either irritative or obstructive, or a combination of both. It varies from frequent toilet visiting and nocturia to restricted urinary flow. These toxic symptoms usually disappear within a year [1,6—9], although longer recoveries and late symptom flare have also been reported [2,10].

There are two possible causes for post-implant LUTS. Firstly, the implantation procedure itself. Implantation needles are inserted through the perineum into the prostate, possibly causing trauma in the functional genitourinary anatomy. Secondly, the irradiation dose deposited by the I-125 sources. High doses to urethra and bladder could possibly cause or contribute to urinary morbidity. However, the dose accumulates rather slowly and only after 60 days half of the total dose will be delivered. It is therefore unlikely that dose related complications occur shortly after the implantation.

Although some studies showed correlations between dose and implant related parameters and LUTS, other studies did not, or found different predictors [1,3—9,11—17]. Most frequently reported predictor however is the prostate volume before implantation [7,8,13,14,18,19]. Many studies concentrated on the dose to the urethra but the dose to the bladder has been ignored so far. Probably the bladder is not regarded an organ at risk because it is not within the implanted area as are prostate and urethra. Nevertheless, the bladder wall and the bladder neck play an important role in the urinary flow regulation and although the average dose to the bladder is always very low, hotspots can occur close to cranially placed seeds. Only Williams et al. [9] reported a positive correlation between LUTS and the number of seeds

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implanted superior to the base of the prostate, suggesting that the dose to the bladder could be an important factor.

In order to remain an attractive treatment modality for localized prostate cancer in the future it is important to reduce side effects of seed implants like LUTS as much as possible. To be able to develop less toxic implantation techniques it is mandatory to identify the risk factors. The purpose of this study was to investigate possible correlations between LUTS recorded at two different time intervals after implantation and implant related parameters with special attention to the dose to the bladder.

Materials and methods

Patients and implants

The study refers to 115 patients treated with permanent brachytherapy of the prostate in our department in the period June 2002–June 2006. In all cases the specified dose was 145 Gy and no external beam radiotherapy was added. Clinical characteristics: tumour stage < T2c, PSA < 10, Gleason score < 7. Excluded from this treatment were patients with an IPSS > 12 and prostate volumes larger than 60 cm^3. Favourable patients with prostates larger than 55 cm^3 were pre-treated with androgen ablation. Between 50 and 100 I-125 seeds were implanted. All patients received 0.4 mg Tamsulosin (alpha blocker) once daily during the first 6 months after treatment. The seeds used were Oncura Rapid Strands model 6711 with a source strength of 0.55 ± 0.02 $\mu Gy\ h^{-1}\ m^2$.

Peripheral seed loading with additional seeds closer to the centre of the prostate was applied in order to achieve adequate dose coverage of the prostate, i.e. to aim at a minimal peripheral dose of 145 Gy. Seed positions were allowed up to 5 mm outside the prostate gland and were not allowed to be closer than 5 mm from the urethra. The average and 1SD of prostate volume, number of implanted seeds and implantation needles were 41 ± 11 cm^3, 81 ± 13 and 26 ± 5, respectively.

Urinary symptom scores

For the scoring of LUTS experienced by patients after implantation of the prostate we used the International Prostate Symptom Score (IPSS) questionnaire [20]. It consists of 7 questions relating to irritative complaints and obstructive urinary flow. The score per question with increasing severity ranges from 0 to 5. That is, in case of no complaints IPSS = 0, in case of maximum severity IPSS = 35. Questionnaires were filled in by 72 patients before implantation (IPSS-0) and at least once after implantation. 59 of these 72 patients filled in the questionnaire at 3 months (IPSS-3m) and 56 patients at 6 months (IPSS-6m) after implantation, i.e. 43 patients filled in the questionnaire both at 3 months and 6 months after implantation. The average and 1SD time span between implantation and IPSS-3m was 90 ± 27 days and between implantation and IPSS-6m 180 ± 26 days.

Early urinary symptom categories

Of the total group of 115 patients, 15 patients suffered from acute urinary retention (AUR) of more than 200 cm^3. These patients depended on a urinary catheter for several days to several weeks after implantation. AUR and high IPSS-3m were both considered to be early urinary symptoms. There were no patients with AUR included in the sub-group of 59 IPSS-3m measurements. In order to avoid double counting in the ''early symptom category'' and any influence of prolonged catheter dependency on the IPSS at 3 months, we excluded the available IPSS-3m scores of AUR patients from the analyses.

We joined the cases with registered AUR and IPSS-3m and stratified this combined group ($n = 59 + 15 = 74$) in two categories. (1) Severe early LUTS ($n = 34$): IPSS-3m $\geqslant 18$ (high absolute score) and IPSS-3m $-$ IPSS-0 $\geqslant 11$ (high increase), or AUR. (2) Mild early LUTS ($n = 40$): other patients within this group. The division between severe and mild was quite arbitrary but an IPSS-3m of at least 18 points is considered to be high by our physicians. Eighteen points is also just over half the maximum score (35 points). A rise of 11 points or more (IPSS-3m minus IPSS-0), the second requirement for severe symptom stratification was chosen because it was at least 1 point over the average rise.

Of 41 patients (115 minus 74) no or incomplete early symptom scores or post-implant dosimetric data were available and could therefore not be included in the early symptom group.

Imaging and dosimetry

One day after implantation a simultaneously acquired CT and 3D transrectal ultrasound (TRUS) scan was made. The method and technical specifications have been described in detail previously [21]. Using the favourable characteristics of these image modalities, the TRUS images were used for the delineation of the prostate, the CT images for the delineation of the bladder wall (including the bladder neck) and the urethra and for the reconstruction of the seeds. The normally difficult to distinguish interface between the base of the prostate and the bladder neck was optimally determined by simultaneous viewing of registered CT and TRUS images. The urethra was made visible by a transurethral urinary catheter. Delineated was the urethra within the prostate boundaries.

In Table 1 the investigated parameters of prostate and implant characteristics in relation to LUTS are described. Previous research showed that the dose–volume parameters of the bladder wall based on a scan made 1 day after implantation differed from those based on a scan 1 month after implantation or later [22]. Therefore we also determined dose volume parameters of the bladder wall based on a scan made 1 month after implantation. From the same study we know that urethra high dose values are underestimated when based on a day-1 scan. However, they do correlate very well with values based on a scan made 1 month after implantation. Therefore we did not consider the rather demanding insertion of a urinary catheter, necessary for the discrimination of the urethra, during the scan at 1 month. Since the D90 of the prostate did not significantly change with scan date, we only used the day-1 value in the analyses.

Because trauma sensitivity of the bladder neck was expected, the number of seeds within a radius of 15 mm from the ostium urethrae internum was counted on the CT made 1 day after implantation (Seeds-BN).