Original Research

Sexual function after permanent $^{125}$I-brachytherapy for prostate cancer

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We prospectively assessed patients’ erectile function (EF) using the International Index of Erectile Function (IIEF) and a global assessment questionnaire (GAQ) following permanent $^{125}$I-brachytherapy for localized prostate cancer. Of 378 treated patients, 220 had a minimal 2-y follow-up and 131/220 were sexually active prior to brachytherapy, with an EF domain score of $\geq 11$ (study group). Patients were allowed sildenafil at any time of the study. The patients’ mean EF score, without excluding patients who used sildenafil, dropped within 3 months after brachytherapy, recovered at the end of the first year and remained unchanged for at least up to 2 y after treatment regardless of the addition of neoadjuvant hormone therapy to $^{125}$I-brachytherapy. Analysis of the GAQ revealed that 80% of the patients were satisfied with their sexual function up to 3 y after treatment. Any detrimental effect of permanent brachytherapy with or without the addition of hormone therapy on EF is reversible, and recovery is expected at 1 y after treatment in most patients.

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Keywords: erectile function; brachytherapy; prostate cancer

Introduction

Erectile dysfunction (ED) is a major concern among men undergoing curative treatment for localized prostate cancer. In the absence of larger studies and longer follow-up periods, it is not clear as to what extent ED is present following prostate brachytherapy. Reports from the literature show that 6–53% of patients could develop ED after permanent seed implantation.1–8 These reported wide ranges of ED probably reflect differences in the length of follow-up, patient selection and the mode of data collection. In general, the series with longer follow-up periods show lower rates of potency preservation.9–71 In a series on brachytherapy using a patient-administered, validated quality-of-life instrument (the specific erectile questions of the International Index of Erectile Function; IIEF), 52% of patients who underwent monotherapy brachytherapy main-
questionnaire that consisted of the five domains of the IIEF as well as a global assessment questionnaire (GAQ). We also compared the outcome of patients who received neoadjuvant hormone therapy in combination with brachytherapy with those who received brachytherapy alone and evaluated the effects of multiple clinical and treatment parameters on penile EF.

Materials and methods

Patients

In all, 378 patients underwent permanent prostate brachytherapy in our department from May 1998 to December 2003 using 125I for localized adenocarcinoma of the prostate gland (clinical stage T1c–T2b). They had a Gleason score \( \leq 7 \), a prostate-specific antigen (PSA) level \(< 20 \text{ng/ml}\) and a life expectancy of at least 10 y. A total of 220 patients had a minimal follow-up of 2 y. High-risk patients (Gleason score 7) who received combined therapy with external-beam radiation were excluded from this study. Patients with a gland \( \geq 50 \text{cm}^3 \) were administered combined androgen blockade for an average of 4 months (range 3–6 months) to reduce the gland size to an acceptable volume of \(< 50 \text{cm}^3\). Hormonal therapy was stopped just before implantation. All patients completed a baseline IIEF questionnaire before treatment. The men who underwent combined brachytherapy and neoadjuvant hormonotherapy completed the questionnaire before the initiation of hormonal treatment.

Brachytherapy

Brachytherapy was performed using either the preplanning or the ‘real-time’ intraoperative method as described previously.\(^{23,24}\) Patients were scheduled to receive a target-matched peripheral dose of 145 Gy (preplan method) or 160 Gy (intraoperative method) according to the American Association of Physicists in Medicine Task Group 43 guidelines.\(^{25}\) All underwent a computed tomography (CT)-based postimplant dosimetry evaluation at 1 month. The same investigators determined all prostate volumes and relevant urethral surfaces. The actual dose distribution to the prostate and urethra was generated by dedicated treatment-planning computer software run by the radiation physicist and oncologist.

All patients were pretreated with an alpha-blocker 1 week prior to implant and for at least 1 month afterwards. During the follow-up visit, patient information with regard to the use of alpha-blockers and urinary disturbances was gathered. All men had to complete the International Prostate Symptom Score (IPSS) questionnaire. Either implant techniques were associated with very low urinary retention rates or other grade 3 or greater urologic morbidity.\(^{23}\) Almost all men had worse urinary symptoms for the first 6 to 9 months. The IPSS returned to preimplant values (±1 point) within 9 to 18 months.\(^{23}\)

Follow-up and assessment of EF

Using the IIEF survey, potency was defined as an EF domain score of \( \geq 11 \) (maximum score 30). Brachytherapy-only patients completed the IIEF questionnaire at 3 months and every 3 months after implantation for the first 2 y. Patients who received neoadjuvant hormone therapy completed the IIEF questionnaire 6 months after implantation and every 3 months thereafter for the first 2 y, since long-term hormonal effects were expected up to 6 month after cessation. Patients with ED for whom there were no contraindications for taking sildenafil were offered escalating doses of the drug (25–100 mg) until satisfaction at any time after treatment. At the end of each year of follow-up, a GAQ evaluated patients’ overall sexual satisfaction. Patients were asked: ‘Are you able to have successful intercourse as before treatment?’ Patients who replied in the affirmative were asked specifically whether their success was achieved spontaneously or with the use of sildenafil. Patients who replied negatively were asked whether they used sildenafil and failed or if they were not interested in trying that treatment. Patients who did not respond to sildenafil and wished to pursue therapeutic measures for their ED were referred to our ED clinic to be evaluated for other treatment modalities, such as intracavernosal injections, vacuum device, etc.

Statistical analysis

The clinical parameters evaluated included age, clinical T stage, Gleason score, pre- and postimplant IIEF and ultrasound-determined prostate volume. Statistical analysis was performed using one- and two-way analysis of variance (ANOVA). Differences were considered significant when \( P < 0.05 \).

Results

Out of 220 patients with at least 2 y of follow-up, we identified 131 patients with a median follow-up of 3 y (range 2–5 y) who were potent before implanta-
tion (EF score ≥11) and they were selected to assess the long-term brachytherapy effect on EF. In order to determine whether there were adverse effects on sexual function by the addition of hormonal treatment, these patients were subdivided into two groups: 80 patients who were treated solely with brachytherapy formed Group 1 and 51 patients who received downsizing neoadjuvant hormone therapy formed Group 2. A comparison of the basic characteristics revealed that the two study groups were not significantly different except for the parameter of prostate size (Table 1).

As shown in Figure 1, there was a significant reduction (\(P<0.01\)) in EF 3 months after brachytherapy among the patients of Group 1. EF in Group 2 was first evaluated after 6 months of brachytherapy (see ‘Materials and methods’), and it was significantly lower (\(P<0.05\)) than that of Group 1 (Figure 1). Recovery from the impairment in EF was slower among patients of Group 2 compared with Group 1 (Figure 1), while there was no longer any significant difference (\(P>0.05\)) in the outcome of EF scores between the two groups at the 1-y follow-up. A 25% decrease in the mean EF score was observed in both groups after 2 y of follow-up. Patients who received neoadjuvant hormone therapy for downsizing are expected to have longer recovery time to reach steady-state measures of EF.

Since there was no significant difference between the two groups in EF at the end of the first year of follow-up, we analyzed the data of the EF and the other four domains of the IIEF questionnaire of all patients at 1 and 2 y of follow-up (Table 2). There was a significant decline (20 to 25%) in all domains 2 y after treatment with the exception of sexual desire. Interestingly, and in contrast to earlier reports on EF after brachytherapy or after radical prostatectomy, the extent to which the EF score decreased (25%) was almost the same among patients with any pretreatment levels of EF score (data not shown). Moreover, there was no correlation between EF score outcome and age, prostate volume, clinical stage, PSA level or Gleason score.

Analysis of the GAQ revealed that 45 to 50% of patients reported satisfaction from their sexual performance without any medications up to 3 y after treatment (Figure 2). An additional 30% of the patients were also satisfied from their sexual function with pharmacologic support (sildenafil), which yields a total of 75–80% of all study patients who were satisfied from their sexual function 1–3 y after brachytherapy. We analyzed the IIEF scores of both patients who claimed potent before and remained so after brachytherapy and patients who claimed potent prior to brachytherapy and consequently needed sildenafil to maintain potency (Table 3). The same pattern of decrease in IIEF domain scores was observed among patients who did or did not need to use sildenafil to maintain potency (Table 3). The results presented in Table 3 show that in spite the use of sildenafil, mean EF scores of patients using sildenafil were lower compared with mean EF scores of patients who did not. EF recovery following various doses of sildenafil (25–100 mg) was observed in 85% of the patients who reported having ED after brachytherapy.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Basic characteristic of the study groups</th>
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<tbody>
<tr>
<td></td>
<td>Group 1</td>
</tr>
<tr>
<td>No.</td>
<td>80</td>
</tr>
<tr>
<td>Age (y)</td>
<td>Mean±s.d.</td>
</tr>
<tr>
<td>Range</td>
<td>51–79</td>
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<tr>
<td>PSA (ng/ml)</td>
<td>Mean±s.d.</td>
</tr>
<tr>
<td>Range</td>
<td>2.47–20</td>
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<tr>
<td>Prostate volume at treatment (cm³)</td>
<td>Mean±s.d.</td>
</tr>
<tr>
<td>Gleason score (% of patients)</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>42</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
</tr>
<tr>
<td>Clinical stage (% of patients)</td>
<td>T1c</td>
</tr>
<tr>
<td></td>
<td>T2a–b</td>
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</table>

Group 1: Brachytherapy only.
Group 2: Brachytherapy with neoadjuvant hormone therapy.
s.d., standard deviation; PSA, prostate-specific antigen; NS, not significant.

Figure 1 Mean EF score of the 131-patient study cohort. Group 1 represents patients (n=80) who received brachytherapy only. Group 2 represents patients (n=51) who received hormone therapy prior to brachytherapy. EF, erectile function domain of the IIEF questionnaire; s.e., standard error of the mean.
Although we did not evaluate factors affecting the response to sildenafil, our impression is that post-implant responses to sildenafil were not dependent on preimplant potency, since many patients who had severe ED prior to brachytherapy responded successfully to sildenafil administration as well (data not shown). This fact further supports the contention that brachytherapy does not negatively affect EF in most patients. Noteworthy, 10–20% of patients with postbrachytherapy ED were not interested in any treatment modalities to improve their sexual function.

Discussion

Prostate brachytherapy with permanent radioactive implants has recently gained popularity among patients undergoing potentially curative treatment for localized prostate cancer. Compared with other alternative treatment options, brachytherapy is associated with sexual function preservation and a lower incidence of untoward side effects. Potency preservation is one of the major considerations in the treatment of localized prostate cancer. In this report, we presented the effect of brachytherapy on EF and overall sexual satisfaction 3 y postimplant in men who were sexually active prior to treatment. The wide range of ED reported after brachytherapy may be related to differences in the instruments that had been used to collect data, the definitions of potency and the length of the follow-up periods. There is subjective difficulty in evaluating patients’ sexual function since the influence on EF is part of the major side effects of treating patients for localized prostate cancer. Another significant issue among patients is the easier exposure to oral medications such as sildenafil whether prescribed by general practitioners or urologists. We used the IIEF questionnaire and a GAQ to prospectively assess EF and sexual satisfaction among potent patients. The IIEF data indicated that there had been a global decrease in all domains of the IIEF score 2 y after brachytherapy (Figure 1 and Table 2). As expected, there was only a slight decrease in the mean SD score, which, although significant, it was not clinically relevant. The effect of brachytherapy on EF was gradual with time and also included recovery of function, unlike radical prostatectomy where the effect is immediate or external-beam radiation where EF declines between 12 and 24 months after irradiation. The initial decline in EF may be attributed to pain in general, discomfort and painful ejaculation since only 25% of the calculated radiation is being emitted within 3 months postimplant. Although the accumulative radiation effect of brachytherapy is expected at the end of the first year of treatment, there was no further deteriorative effect in EF among our patients. The effect of neoadjuvant hormone therapy was transient, and there was no significant difference between the patients who received brachytherapy alone or those who received the addition of neoadjuvant hormone therapy.

Table 2  IIEF scores before and after brachytherapy of 131 study patients

<table>
<thead>
<tr>
<th>Domain</th>
<th>Score range</th>
<th>Before brachytherapy, mean ± s.d.</th>
<th>1 y after brachytherapy, mean ± s.d.</th>
<th>2 y after brachytherapy, mean ± s.d.</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF</td>
<td>1–30</td>
<td>22.5 ± 6</td>
<td>14.7 ± 10</td>
<td>16.8 ± 10</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>OF</td>
<td>0–10</td>
<td>7.3 ± 2.8</td>
<td>4.9 ± 3.6</td>
<td>5.6 ± 3.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>SD</td>
<td>2–10</td>
<td>7.2 ± 1.5</td>
<td>5.5 ± 2.3</td>
<td>6.0 ± 2.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IS</td>
<td>0–15</td>
<td>11.0 ± 2.7</td>
<td>7.3 ± 5</td>
<td>8.1 ± 4.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>OS</td>
<td>2–10</td>
<td>8.1 ± 1.9</td>
<td>5.8 ± 3.0</td>
<td>6.3 ± 2.8</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Results represent mean scores of all study patients including those who were using sildenafil (90%). P-value represents significance between pretreatment measures compared with 1 or 2 y after treatment. s.d., standard deviation; IIEF, International Index of Erectile Function; EF, erectile function; OF, orgasmic function; SD, sexual desire; IS, intercourse satisfaction; OS, overall satisfaction.

Figure 2  Distribution of patients according to the GAQ analysis. Analysis was performed using the records of the study patients who replied to a GAQ 1 y (n = 112), 2 y (n = 108) and 3 y (n = 30) after treatment. (a) Patients who were unable to have successful intercourse as before brachytherapy. (b) Patients who were able to have successful intercourse after brachytherapy. (c) patients who were able to have successful intercourse after brachytherapy using sildenafil. (d) Patients who were unable to have successful intercourse after brachytherapy and did not respond to sildenafil treatment.

Although we did not evaluate factors affecting the response to sildenafil, our impression is that post-implant responses to sildenafil were not dependent on preimplant potency, since many patients who had severe ED prior to brachytherapy responded successfully to sildenafil administration as well (data not shown). This fact further supports the contention that brachytherapy does not negatively affect EF in most patients. Noteworthy, 10–20% of patients with postbrachytherapy ED were not interested in any treatment modalities to improve their sexual function.
hormonal treatment at the end of the first year of follow-up (Figure 1). As expected, androgen ablation using LH-RH agonists was associated with a significant loss of EF, but it was reversible. Androgen ablation was apparently responsible for the profoundly decreased sexual function among patients who received the combined treatment, similar to the findings reported by others.\(^{20-32}\) Therefore, patients who are receiving hormonal treatment should be well informed about the possibility of such occurrences.

Long-term studies on potency after prostate brachytherapy are not yet conclusive. Reports with longer follow-up indicate a decline in potency preservation over time.\(^{9-11}\) Our prospectively collected data show that after 3 y of follow-up most patients were content with their sexual performance, whether they maintained their EF with or without the support of oral sildenafil (Figure 2). Our results show that potency rates remained in the 50–85% range, concurrent with early follow-up reported series.\(^{7,32,33}\) It is important to take into account that the IIEF scores (Figure 1, Tables 2 and 3) and the overall satisfaction (Figure 2) of our patients may have been positively affected by the use of sildenafil. Even longer than the 3 y prospective follow-up of our patients would reveal whether there will be an additional decline in EF as previously reported in the mostly retrospective literature.

The mechanism of ED following brachytherapy is not clear, but the radiation dose to the neurovascular bundle has been implicated in some studies.\(^{34,35}\) where potency preservation was highly dependent on pretreatment potency and age, the decline in the mean EF score of our study patients was not correlated with either pretreatment EF status or age. Moreover, the high response rates (83–86%) to sildenafil after brachytherapy among our patients renders brachytherapy beneficial from the aspect of quality of life, compared to radical prostatectomy where successful treatment of ED with sildenafil depends on the preservation of the neurovascular bundles, with overall lower response rates (50–80%).\(^{36-42}\)

Whether a further decline in potency as a function of time following brachytherapy is to be expected and which of the patients would be more susceptible to these long-term effects await elucidation. The response rate to sildenafil with time is also undetermined.

### Conclusions

The reported potency rates after prostate brachytherapy are high. A 3-y follow-up demonstrated some decrease in the potency rate but the majority of the patients (up to 80%) were able to have adequate erections for satisfactory sexual activity with or without sildenafil. Longer follow-up assessment of EF will help to better understand the changes that occur with time after brachytherapy, to develop methods for better defining patients who are at higher risk of becoming impotent and to compare them with the natural history of EF in age-matched men.

### Acknowledgements

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### References

Sexual function post prostate brachytherapy


Kiteley RA et al. Radiation dose to the neurovascular bundles or penile bulb does not predict erectile dysfunction after prostate brachytherapy. Brachytherapy 2002; 1: 90–94.

Albert M et al. Late genitourinary and gastrointestinal toxicity after magnetic resonance image-guided prostate brachytherapy with or without neoadjuvant external beam radiation therapy. Cancer 2003; 98: 949–954.


