

HEALTH-RELATED QUALITY OF LIFE UP TO SIX YEARS AFTER ¹²⁵I BRACHYTHERAPY FOR EARLY-STAGE PROSTATE CANCER

ELLEN M. A. ROELOFFZEN, M.D.,* IRENE M. LIPS, M.D.,* MARION P. R. VAN GELLEKOM, PH.D.,*
JOEP VAN ROERMUND, M.D.,† STEVEN J. FRANK, M.D.,‡ JAN J. BATTERMANN, M.D., PH.D.,*
AND MARCO VAN VULPEN, M.D., PH.D.*

Departments of *Radiation Oncology and †Urology, University Medical Center Utrecht, Utrecht, The Netherlands; and ‡Department of Radiation Oncology, M. D. Anderson Medical Center, Houston, TX

Purpose: Health-related quality of life (HRQOL) after prostate brachytherapy has been extensively described in published reports but hardly any long-term data are available. The aim of the present study was to prospectively assess long-term HRQOL 6 years after ¹²⁵I prostate brachytherapy.

Methods and Materials: A total of 127 patients treated with ¹²⁵I brachytherapy for early-stage prostate cancer between December 2000 and June 2003 completed a HRQOL questionnaire at five time-points: before treatment and 1 month, 6 months, 1 year, and 6 years after treatment. The questionnaire included the RAND-36 generic health survey, the cancer-specific European Organization for Research and Treatment of Cancer core questionnaire (EORTCQLQ-C30), and the tumor-specific EORTC prostate cancer module (EORTC-PR25). A change in a score of ≥ 10 points was considered clinically relevant.

Results: Overall, the HRQOL at 6 years after ¹²⁵I prostate brachytherapy did not significantly differ from baseline. Although a statistically significant deterioration in HRQOL at 6 years was seen for urinary symptoms, bowel symptoms, pain, physical functioning, and sexual activity ($p < .01$), most changes were not clinically relevant. A statistically significant improvement at 6 years was seen for mental health, emotional functioning, and insomnia ($p < .01$). The only clinically relevant changes were seen for emotional functioning and sexual activity.

Conclusion: This is the first study presenting prospective HRQOL data up to 6 years after ¹²⁵I prostate brachytherapy. HRQOL scores returned to approximately baseline values at 1 year and remained stable up to 6 years after treatment. ¹²⁵I prostate brachytherapy did not adversely affect patients' long-term HRQOL. © 2010 Elsevier Inc.

Long-term, health-related quality of life, HRQOL, prostate cancer, ¹²⁵I brachytherapy, European Organization for Research and Treatment of Cancer prostate cancer module.

INTRODUCTION

Iodine-125 (¹²⁵I) brachytherapy for early-stage prostate cancer shows excellent tumor control and survival rates (1–4). The results are equivalent to those achieved by radical prostatectomy or external beam radiotherapy (5). Hence, toxicity and health-related quality of life (HRQOL) are considered important endpoints that should be taken into account in the decision of a treatment modality.

Although many studies have reported HRQOL after ¹²⁵I prostate brachytherapy (6–15), most were limited by being cross-sectional, by having a short duration of follow-up, or by lacking extended and validated HRQOL questionnaires. Because long-term side effects can occur >3 years after treatment (16), long-term follow-up of HRQOL is required. Furthermore, a baseline QOL measure is required to analyze

QOL changes over time. To the best of our knowledge, no study has prospectively analyzed HRQOL ≥ 2 years after ¹²⁵I prostate brachytherapy.

Some reports have described long-term prostate symptom scores such as the International Prostate Symptom Score (IPSS). Ash *et al.* (15) reported that IPSS scores 9 years after treatment did not differ compared with the baseline IPSSs. However, in addition to somatic functioning, HRQOL also includes patients' perceptions of their social and psychological functioning and well-being (17, 18). An appraisal of physical and psychosocial complications after prostate cancer treatment can differ when evaluated by patients or physicians (19). Therefore, HRQOL assessments should be performed using internationally validated questionnaires (20, 21).

Note—An online CME test for this article can be taken at <http://astro.astro.org> under Continuing Education.

Reprint requests to: Ellen Roeloffzen, M.D., Department of Radiation Oncology, University Medical Center Utrecht, Heidelberglaan 100, Utrecht 3584 CX The Netherlands. Tel: (+31) 88-

755-8800; Fax: (+31) 88-755-5850; E-mail: E.M.A.Roeloffzen@UMCUtrecht.nl

Conflict of interest: none.

Received Feb 10, 2009, and in revised form March 11, 2009. Accepted for publication March 16, 2009.

Previously, we published our HRQOL data of 127 patients treated with ^{125}I brachytherapy for localized prostate cancer up to 1 year after treatment (22). In the present study, we present the long-term HRQOL outcomes 6 years after implantation.

METHODS AND MATERIALS

Patients

Between December 2000 and June 2003, 127 patients with localized prostate cancer were treated with monotherapeutic ^{125}I brachytherapy at our department according to the European Association of Urology guidelines (2, 22, 23). The patient characteristics are listed in Table 1. Six months of neoadjuvant hormonal treatment with a luteinizing hormone-releasing hormone agonist was given to patients presenting with a prostate volume $>50\text{ cm}^3$ ($n = 28$).

Treatment

The treatment technique used has been previously described (2, 22). Transrectal ultrasonography-guided transperineal permanent ^{125}I seed implantation was performed using a real-time intraoperative-planned approach with the Sonographic Planning of Oncology Treatment system (Nucletron BV, Veenendaal, The Netherlands). From 2002, the Fully Integrated Real-time Seed Treatment system was used (Nucletron BV, Veenendaal, The Netherlands). The planned dose to the prostate was 144 Gy, according to the guidelines of the Radiation Therapy Committee Task Group No. 43 of the American Association of Physicists in Medicine (24). At 4 weeks after implantation, all patients underwent radiography, computed tomography, and magnetic resonance imaging for postplanning evaluation.

QOL assessment

All 127 patients received a HRQOL questionnaire at several time-points: before treatment (baseline) and 1 month, 6 months, and 1 year after treatment. These points corresponded to the follow-up visits at our department. In July 2008, all previously evaluated patients were contacted again after a median follow-up of 6.4 years (range, 5.3–7.7). Of the 127 patients, 102 returned a completed questionnaire. Of the 25 nonresponders, 15 had died, 7 were lost to follow-up, and 3 refused to complete the questionnaire.

The questionnaire included the RAND-36 generic health survey (25), the cancer-specific European Organization for Research and Treatment of Cancer core questionnaire (EORTC QLQ-C30) (17), and the tumor-specific EORTC prostate cancer module (EORTC QLQ-PR25) (26).

The RAND-36 health survey (25) contains four functional scales (physical role restriction, social role restriction, physical problems, and emotional problems). Also, three items concerning well-being (mental health, vitality, and pain) and two items for general health (general health experience, change in health) are evaluated. All scales of the RAND-36 range in score from 0 to 100, with a greater score indicating better HRQOL.

The EORTC QLQ-C30 (17) contains five functional scales (physical, role emotional, cognitive, and social), a global HRQOL scale, three symptom scales (nausea and vomiting, fatigue, and pain), and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). The EORTC QLQ-PR25 (26) contains five scales (urinary symptoms/problems, bowel symptoms/problems, treatment-related symptoms, sexual functioning, and sexual activity). All scales of the EORTC QLQ-C30 and the EORTC QLQ-PR25 range in score from 0 to 100. For the functional scales and the global QOL scale, a higher score represents

Table 1. Patient characteristics ($n = 127$)

Characteristic	Value
Age at implantation (y)	
Mean	65
Range	50–78
Tumor stage (n)	
T1b	1 (0.8)
T1c	82 (65)
T2a	43 (34)
T2b	1 (0.8)
Gleason sum-score (n)	
2–6	55 (43)
7	72 (57)
Pretreatment PSA (ng/mL)	
Mean	10.1
Range	1.7–38
Pretreatment TURP (n)	
Yes	2 (2)
No	125 (98)
Neoadjuvant hormonal therapy (n)	
Yes	28 (22)
No	99 (78)
Mean pretreatment prostate volume (cm^3)	37.8 ± 11.4

Abbreviations: PSA = prostate-specific antigen; TURP = transurethral resection of prostate.

Data in parentheses are percentages.

a greater level of functioning or global HRQOL. For symptom scales and single items, higher scores indicate more symptoms or more problems.

All questionnaires are well validated and widely used in oncology trials. According to the published data concerning the interpretation of HRQOL data, a change of ≥ 10 points on a 100-point scale was considered clinically relevant (27).

Statistical analysis

The scores of the RAND-36, EORTC QLQ-C30, and EORTC QLQ-PR25 QOL items were computed. Descriptive statistics (mean, range, and confidence intervals) were used to assess the patient characteristics. Differences in HRQOL between baseline and the follow-up points were analyzed using a paired samples *t* test. Only patients who completed the questionnaires at all time-points were included in the analysis.

Cronbach's α coefficients were calculated to determine internal consistency reliability of the questions. The reference value of Cronbach's α coefficient for sufficient internal consistency was ≥ 0.70 . Reliability analysis resulted in a Cronbach's α coefficient of ≥ 0.70 for all HRQOL items, except for nausea and vomiting in the EORTC QLQ-C30 and bowel and treatment-related symptoms in the EORTC QLQ-PR25. This is in accordance with the findings from a recent study by van Andel *et al.* (28) demonstrating acceptable psychometric properties and clinical validity for the EORTC QLQ-PR25, except for bowel function and side effects of hormonal therapy scales.

To assess whether any clinical characteristic could predict the HRQOL at 6 years after treatment, univariate and multivariate linear regression analyses were applied. The pretreatment clinical factors included in the analysis were age, neoadjuvant hormonal therapy, initial prostate-specific antigen level, and prostate volume. Predictive factors were selected with backward stepwise selection using $p = .20$.

A commercial statistical package (Statistical Package for Social Sciences, version 16.0, SPSS, Chicago, IL) was used for statistical analysis of the data. To account for multiple comparisons, $p \leq .01$ was considered statistically significant.

RESULTS

The mean scores and standard deviations of the HRQOL items at five different points are listed in Table 2. For most items, an increase in symptoms or a decreased level of functioning or QOL was seen 1 month after treatment. Subsequently, the symptoms gradually diminished and the functioning scores improved. Comparing the HRQOL scores at 6 years after treatment with those at baseline resulted in statistically significant differences for several HRQOL items. However, by comparing the HRQOL scores 6 years after treatment with those at 1 year after treatment found no statistically significant differences were found for any of the HRQOL items (data not shown).

A statistically significant deterioration after 6 years compared with baseline was seen for physical functioning, pain, urinary symptoms, bowel symptoms, and sexual activity ($p \leq .01$). A statistically significant improvement after 6 years was seen for mental health, emotional functioning, and insomnia ($p \leq .01$). For all other HRQOL items, no significant difference was seen. The only clinically relevant changes after 6 years were seen for emotional functioning (10-point increase) and sexual activity (15-point decrease).

The most reported adverse events after prostate brachytherapy are urinary and bowel symptoms. Figure 1 shows the mean change over time in the urinary symptom scores (EORTC QLQ-PR25) up to 6 years after ^{125}I prostate brachytherapy. After an initial increase at 1 month after treatment, the urinary symptoms gradually improved and had reached baseline levels at 1 year after treatment. The urinary symptoms then remained stable up to 6 years after treatment. The same trend was seen for the bowel symptom scores (EORTC QLQ-PR25) (Fig. 2). At 6 years after treatment, 36% of the patients had less urinary symptoms compared with baseline, 47% had more urinary symptoms, and 17% had no change in urinary symptoms. For bowel symptoms, 14% of the patients had less symptoms compared with baseline, 32% had more symptoms, and 54% had no change in symptoms.

Figure 3 shows the clinically relevant improvement over time in emotional functioning (EORTC QLQ-C30). The development of sexual activity scores (EORTC QLQ-PR25) over time is shown in Fig. 4. At 6 years after treatment, 70% of the patients had diminished sexual activity compared with baseline, 12% had improved sexual activity, and 18% had no change in sexual activity.

Multivariate linear regression analysis was performed to identify predictors for diminished HRQOL at 6 years after treatment. Predictors for urinary symptoms were hormonal therapy (β , 8.1; 95% confidence interval [CI], -0.07 to 16.2) and initial prostate-specific antigen level (β , -0.19 ; 95% CI, -0.48 to 0.09). Prostate volume (β , 0.11; 95% CI, -0.03 to 0.25) was identified as a predictor for bowel

symptoms. Older age (β , -1.37 ; 95% CI, -2.26 to -0.48) was associated with diminished sexual activity at 6 years. Age (β , -1.50 ; 95% CI, -2.13 to -0.86), hormonal therapy (β , 14.2; 95% CI, 3.8 to 24.6) and initial prostate-specific antigen level (β , -0.53 ; 95% CI, -0.89 to -0.16) were predictors for sexual functioning.

DISCUSSION

To the best of our knowledge, this is the first study prospectively assessing long-term HRQOL after ^{125}I brachytherapy for early-stage prostate cancer. Long-term QOL is required, because toxicity after prostate brachytherapy can develop more than 3 years after treatment (16). In the present study, we compared HRQOL approximately 6 years after treatment with the baseline values. Previously, we published our HRQOL data at up to 1 year after treatment, showing significantly worse HRQOL at 1 month after treatment compared with other points (22). Our long-term data show that overall HRQOL at 6 years after treatment did not differ significantly from that at baseline. Thus, ^{125}I brachytherapy does not adversely affect patients' long-term HRQOL.

Although a statistically significant change between 6 years after treatment and baseline was seen for some HRQOL items, most changes were not clinically relevant. A statistically significant deterioration was seen for urinary symptoms, bowel symptoms, pain, physical functioning, and sexual activity. A statistically significant improvement was seen for emotional functioning, mental health, and insomnia. Only for emotional functioning and sexual activity a clinically relevant change was seen.

In an additional analysis, we compared the HRQOL at 6 years after treatment with that at 1 year after treatment. For none of the investigated HRQOL items was a statistically significant difference found, indicating that the QOL remains stable after 1 year post-treatment. Therefore, our data would suggest that measuring patients' HRQOL after prostate brachytherapy could be limited to 1 year after treatment. However, these data need to be confirmed.

Urinary dysfunction is the most common adverse event associated with prostate brachytherapy. The increase in symptoms 1 month after treatment has been frequently described (6, 15, 22). Figure 1 shows that 1 year post-treatment the urinary symptoms had returned to approximately baseline level and remained stable for up to 6 years after treatment.

Although numerous studies have reported the short-term urinary symptoms after prostate brachytherapy, to date, only a few studies have evaluated the long-term urinary QOL (8, 12, 15, 29). Ash *et al.* (15) described the IPSS scores up to 9 years after ^{125}I brachytherapy. However, HRQOL is a multidimensional concept that includes more than toxicity alone (17, 18). The more extended Expanded Prostate Cancer Index Composite urinary symptom scores were also evaluated but were limited by a short follow-up of 2 years. At 1 year after treatment, the mean Expanded Prostate Cancer Index Composite score had returned to the pretreatment level. This finding is similar to the results from Merrick *et al.* (8),

Table 2. Mean scores ± standard deviation of HRQOL items at different time-points before and after ¹²⁵I prostate brachytherapy

Variable	Baseline (n = 127)	1 mo (n = 125)	6 mo (n = 118)	1 y (n = 91)	6 y (n = 102)	Difference between baseline and 6y (p-value)
RAND-36						
Physical functioning	89 ± 14	84 ± 19	85 ± 19	87 ± 16	84 ± 20	.01*
Social functioning	86 ± 18	73 ± 23	83 ± 20	88 ± 17	88 ± 17	NS
Physical role restriction	84 ± 31	64 ± 41	74 ± 37	77 ± 37	84 ± 34	NS
Emotional role restriction	80 ± 32	78 ± 36	82 ± 33	91 ± 23	88 ± 28	NS
Mental health	77 ± 17	79 ± 16	81 ± 14	81 ± 15	82 ± 14	.004*
Vitality	70 ± 19	67 ± 21	69 ± 18	70 ± 19	72 ± 16	NS
Pain	94 ± 13	82 ± 19	87 ± 19	90 ± 17	91 ± 15	.003*
General health	69 ± 15	67 ± 17	68 ± 19	67 ± 18	70 ± 17	NS
Change in health	47 ± 17	41 ± 17	47 ± 19	56 ± 19	50 ± 12	NS
EORTC QLQ-C30						
Physical functioning	92 ± 12	90 ± 13	89 ± 14	90 ± 13	88 ± 14	.006*
Role functioning	92 ± 17	79 ± 25	85 ± 21	88 ± 20	89 ± 20	NS
Emotional functioning	79 ± 18	84 ± 17	86 ± 16	88 ± 15	89 ± 14	<.001†
Cognitive functioning	86 ± 16	88 ± 16	88 ± 16	88 ± 17	84 ± 21	NS
Social functioning	92 ± 15	81 ± 20	90 ± 15	91 ± 15	94 ± 13	NS
Global health/QOL	80 ± 14	73 ± 16	76 ± 16	78 ± 16	82 ± 12	NS
Fatigue	19 ± 19	25 ± 22	23 ± 20	20 ± 19	22 ± 19	NS
Nausea and vomiting	1 ± 5	2 ± 7	2 ± 5	1 ± 4	1 ± 3	NS
Pain	6 ± 14	17 ± 19	14 ± 20	10 ± 18	9 ± 17	.002*
Dyspnea	10 ± 18	12 ± 22	15 ± 22	13 ± 21	10 ± 17	NS
Insomnia	20 ± 27	29 ± 33	21 ± 29	16 ± 25	17 ± 24	.01*
Appetite loss	4 ± 13	3 ± 13	3 ± 12	3 ± 11	2 ± 7	NS
Constipation	2 ± 10	13 ± 24	5 ± 14	4 ± 13	3 ± 9	NS
Diarrhea	6 ± 15	12 ± 21	11 ± 19	6 ± 18	5 ± 15	NS
Financial difficulties	1 ± 5	4 ± 12	3 ± 9	2 ± 8	1 ± 6	NS
EORTC QLQ-PR25						
Urinary symptoms/problems	13 ± 12	40 ± 23	26 ± 18	17 ± 15	18 ± 17	.002*
Bowel symptoms/problems	3 ± 5	8 ± 11	7 ± 10	4 ± 7	6 ± 8	.002*
Treatment-related symptoms	7 ± 9	8 ± 8	9 ± 10	7 ± 8	6 ± 8	NS
Sexual functioning	34 ± 26	25 ± 22	33 ± 24	37 ± 23	39 ± 24	NS
Sexual activity	77 ± 24	61 ± 24	64 ± 27	63 ± 25	62 ± 25	<.001†

Abbreviations: HRQOL = health-related quality of life; RAND-36 = RAND Medical Outcomes Study Short Form 36-item Health Survey; NS = not statistically significant; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer core questionnaire; EORTC QLQ-PR25 = tumor-specific EORTC prostate cancer module.

In RAND-36, higher score represents better health; in EORTC QLQ-C30 and QLQ-PR25, higher score represents more symptoms or better level of functioning or quality of life.

* Statistically significant.

† Clinically relevant (≥10-point difference).

who found no significant difference in long-term urinary QOL when brachytherapy patients were compared with a matched control group. Although that study was limited by its cross-sectional design, the results are similar to our data.

The results from studies that evaluated short-term urinary QOL were similar to ours as well. Lee *et al.* (6) described a return to baseline levels for IPSS and Functional Assessment of Cancer Therapy–Prostate scores 1 year after prostate brachytherapy. Downs *et al.* (9) found a return of University of California, Los Angeles, Prostate Cancer Index scores to baseline at 18–24 months after treatment. Feigenberg *et al.* (10) reported no return of IPSSs to baseline levels 1 year after treatment for 60% of patients. Nevertheless, using the Functional Assessment of Cancer Therapy–Prostate, two-thirds of the men reported urinary function compared with baseline. Only Caffo *et al.* (11) did not found a return to baseline levels for urinary symptoms until 3 years after treatment. Some other published studies were primarily designed to compare different treatment modalities (7, 13, 14, 16).

A difficulty in comparing these studies is the use of different questionnaires, making interpretation of the results a challenge.

Fewer studies have been published concerning bowel symptoms after prostate brachytherapy. In our study, bowel symptoms returned to the baseline level at 1 year and remained stable for up to 6 years after treatment (Fig. 2). Although a statistically significant worsening of symptoms was found at 6 years compared with baseline, no clinically relevant change was seen. However, we must interpret these results with caution, because van Andel *et al.* (28) recently described unsatisfactory clinical validity for the EORTC QLQ-PR25 bowel function item. Also, in our analysis, the Cronbach α coefficient for this item was limited. Despite this possible limitation, our results are in accordance with other published data. Merrick *et al.* (30) demonstrated that prostate brachytherapy adversely affects bowel symptoms in approximately 10% of patients and, in most patients, the changes are minimal and slowly resolve with time. Others

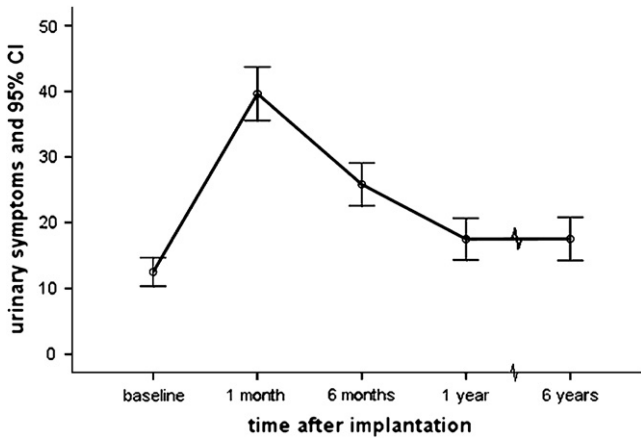


Fig. 1. Urinary symptom scores (mean and 95% confidence intervals (CIs)) of the European Organization for Research and Treatment of Cancer prostate cancer module (EORTC QLQ-PR25) up to 6 years after ¹²⁵I prostate brachytherapy. Higher score represents more symptoms or more problems.

have confirmed the absence of relevant long-term bowel morbidity after prostate brachytherapy (15, 29).

Sexual activity after prostate brachytherapy was also evaluated. A clinically relevant 15-point decrease in sexual activity was seen after 6 years, without a significant worsening in sexual functioning. Feigenberg *et al.* (10) confirmed this discrepancy in sexual functioning and sexual activity. At 1 year, 78% of the patients stated that they could achieve an erection with or without assistance; however, almost 50% reported a decrease in sexual activity (10). This is important, because most studies reporting sexual toxicity after cancer therapies focus only on erectile function. Stock *et al.* (31) reported actuarial decreases in erectile function in 29% of patients 1 year after prostate brachytherapy, and Potters *et al.* (32) reported a potency rate of 67% at 5 years. However, the decrease in sexual activity might be explained, not only by the possibility of achieving an erection, but also by aging, the loss of a partner, or the detrimental effect of cancer treatment on a patient's frequency of sexual activity.

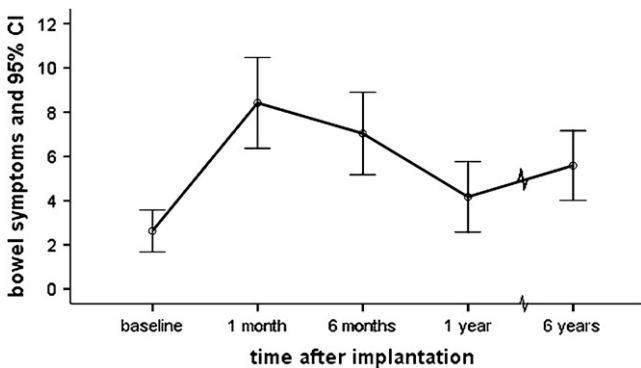


Fig. 2. Bowel symptom scores (mean and 95% confidence intervals (CIs)) of the European Organization for Research and Treatment of Cancer prostate cancer module (EORTC QLQ-PR25) up to 6 years after ¹²⁵I prostate brachytherapy. Greater score represents more symptoms or more problems.

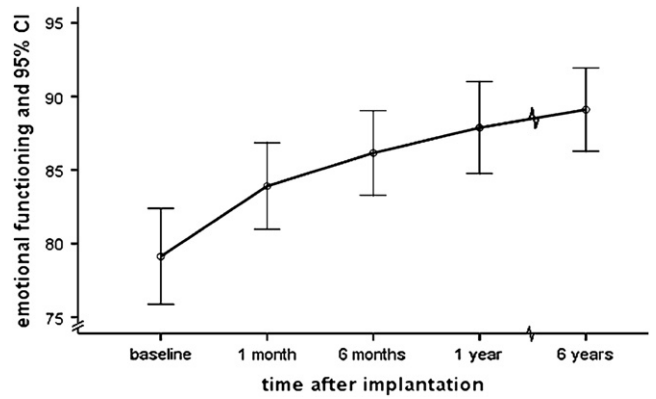


Fig. 3. Emotional functioning scores (mean and 95% confidence intervals (CIs)) of the European Organization for Research and Treatment of Cancer core questionnaire (EORTC QLQ-C30) up to 6 years after ¹²⁵I prostate brachytherapy. Higher score represents greater level of emotional functioning.

As mentioned, in the present study, we did not find long-term sexual dysfunction. This might have been because of our longer follow-up, indicating that improvement in sexual functioning could continue for several years after treatment. Ash *et al.* (15) also found a moderate improvement in sexual function 2 years after prostate brachytherapy. Feigenberg *et al.* (10) demonstrated that the negative effect of prostate brachytherapy on sexuality was significant only in the immediate posttreatment period. Finally, one could argue that the Dutch translation of the EORTC QLQ-PR25 requests an answer to the questions concerning sexual activity only when the patients had been sexually active in the previous 4 weeks, thus causing a low response rate for this scale and perhaps leading to an under- or overestimated QOL in terms of sexual activity. However, in our analysis, the response rate to sexual activity was 71% and was even 100% for sexual functioning.

We found a clinically relevant 10-point improvement in emotional functioning 6 years after prostate brachytherapy.

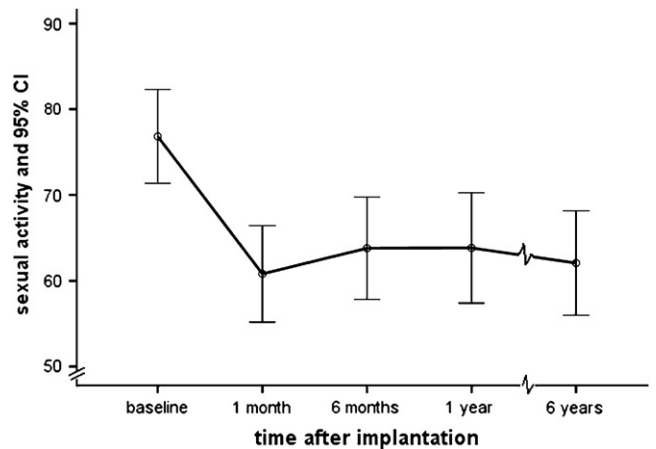


Fig. 4. Sexual activity scores (mean and 95% confidence intervals (CIs)) of the European Organization for Research and Treatment of Cancer prostate cancer module (EORTC QLQ-PR25) up to 6 years after ¹²⁵I prostate brachytherapy. A higher score represents a higher level of sexual activity.

This improvement after cancer therapy has been described for other cancer types as well and can be explained by patients having had time to adapt to the situation, a response shift mechanism, and a decreasing fear of recurrence and death with time (33). The same mechanisms could apply to the statistically significant improvement in mental health.

Although HRQOL at 6 years after treatment was not significantly different compared with baseline for the whole cohort, we found some predictors for diminished HRQOL. In particular, the effect of neoadjuvant hormonal therapy on HRQOL has been questioned in published studies. Our data showed that hormonal therapy seemed to predict for more urinary symptoms and worse sexual functioning at 6 years after treatment. Because our data at 6 years hardly showed any clinically relevant changes in QOL compared with baseline, we did not expect any correlation with dose. Therefore, we did not include dosimetric parameters in the analysis. Acute urinary retention, relapse, and salvage therapy are also factors that might be associated with HRQOL. In ongoing research, we will explore further the predictive factors for short- and long-term HRQOL and validate them.

The present study had several limitations. First, we did not have a control group, which precludes a correction for age-related morbidity. Second, patients received the first questionnaire after their diagnosis. The knowledge of having cancer might have influenced their HRQOL. Third, our study described the experience of a single center. Morbidity might vary from center to center, depending on the treatment techniques used. Fourth, social and demographic items were not evaluated and these might have influenced patients' HRQOL. The study population was a white Dutch population, and the QOL might differ from those of other countries and cultures.

CONCLUSION

This is the first study presenting prospective HRQOL data up to 6 years after ^{125}I prostate brachytherapy. The HRQOL scores had returned to approximately baseline values at 1 year and remained stable up to 6 years after treatment. ^{125}I prostate brachytherapy did not adversely affect patients' long-term HRQOL.

REFERENCES

- Grimm PD, Blasko JC, Sylvester JE, *et al.* 10-Year biochemical (prostate-specific antigen) control of prostate cancer with (125I) brachytherapy. *Int J Radiat Oncol Biol Phys* 2001;51:31–40.
- Battermann JJ, Boon TA, Moerland MA. Results of permanent prostate brachytherapy: 13 years of experience at a single institution. *Radiother Oncol* 2004;71:23–28.
- Zelefsky MJ, Kuban DA, Levy LB, *et al.* Multi-institutional analysis of long-term outcome for stages T1-T2 prostate cancer treated with permanent seed implantation. *Int J Radiat Oncol Biol Phys* 2007;67:327–333.
- Potters L, Morgenstern C, Calugaru E, *et al.* 12-Year outcomes following permanent prostate brachytherapy in patients with clinically localized prostate cancer. *J Urol* 2008;179:S20–S24.
- Peschel RE, Colberg JW. Surgery, brachytherapy, and external-beam radiotherapy for early prostate cancer. *Lancet Oncol* 2003;4:233–241.
- Lee WR, McQuellon RP, Harris-Henderson K, *et al.* A preliminary analysis of health-related quality of life in the first year after permanent source interstitial brachytherapy (PIB) for clinically localized prostate cancer. *Int J Radiat Oncol Biol Phys* 2000;46:77–81.
- Brandeis JM, Litwin MS, Burnison CM, *et al.* Quality of life outcomes after brachytherapy for early stage prostate cancer. *J Urol* 2000;163:851–857.
- Merrick GS, Butler WM, Wallner KE, *et al.* Long-term urinary quality of life after permanent prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 2003;56:454–461.
- Downs TM, Sadetsky N, Pasta DJ, *et al.* Health related quality of life patterns in patients treated with interstitial prostate brachytherapy for localized prostate cancer—Data from CaPSURE. *J Urol* 2003;170:1822–1827.
- Feigenberg SJ, Lee WR, Desilvio ML, *et al.* Health-related quality of life in men receiving prostate brachytherapy on RTOG 98-05. *Int J Radiat Oncol Biol Phys* 2005;62:956–964.
- Caffo O, Fellin G, Bolner A, *et al.* Prospective evaluation of quality of life after interstitial brachytherapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys* 2006;66:31–37.
- Stone NN, Stock RG. Long-term urinary, sexual, and rectal morbidity in patients treated with iodine-125 prostate brachytherapy followed up for a minimum of 5 years. *Urology* 2007;69:338–342.
- Frank SJ, Pisters LL, Davis J, *et al.* An assessment of quality of life following radical prostatectomy, high dose external beam radiation therapy and brachytherapy iodine implantation as monotherapies for localized prostate cancer. *J Urol* 2007;177:2151–2156.
- Litwin MS, Gore JL, Kwan L, *et al.* Quality of life after surgery, external beam irradiation, or brachytherapy for early-stage prostate cancer. *Cancer* 2007;109:2239–2247.
- Ash D, Bottomley D, Al Qaisieh B, *et al.* A prospective analysis of long-term quality of life after permanent I-125 brachytherapy for localized prostate cancer. *Radiother Oncol* 2007;84:135–139.
- Miller DC, Sanda MG, Dunn RL, *et al.* Long-term outcomes among localized prostate cancer survivors: Health-related quality-of-life changes after radical prostatectomy, external radiation, and brachytherapy. *J Clin Oncol* 2005;23:2772–2780.
- Aaronson NK, Ahmedzai S, Bergman B, *et al.* The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85:365–376.
- Penson DF. Quality of life after therapy for localized prostate cancer. *Cancer J* 2007;13:318–326.
- Litwin MS, Lubeck DP, Henning JM, *et al.* Differences in urologist and patient assessments of health related quality of life in men with prostate cancer: Results of the CaPSURE database. *J Urol* 1998;159:1988–1992.
- Henderson A, Andreyev HJ, Stephens R, *et al.* Patient and physician reporting of symptoms and health-related quality of life in trials of treatment for early prostate cancer: Considerations for future studies. *Clin Oncol (R Coll Radiol)* 2006;18:735–743.
- Sloan JA, Frost MH, Berzon R, *et al.* The clinical significance of quality of life assessments in oncology: A summary for clinicians. *Support Care Cancer* 2006;14:988–998.
- van Gellekom MPR, Moerland MA, van Vulpen M, *et al.* Quality of life of patients after permanent prostate brachytherapy in

- relation to dosimetry. *Int J Radiat Oncol Biol Phys* 2005;63:772–780.
23. Ash D, Flynn A, Battermann J, *et al.* ESTRO/EAU/EORTC recommendations on permanent seed implantation for localized prostate cancer. *Radiother Oncol* 2000;57:315–321.
 24. Nath R, Anderson LL, Luxton G, *et al.* Dosimetry of interstitial brachytherapy sources: Recommendations of the AAPM Radiation Therapy Committee Task Group No. 43. American Association of Physicists in Medicine. *Med Phys* 1995;22:209–234.
 25. Hornbrook MC, Goodman MJ. Assessing relative health plan risk with the RAND-36 health survey. *Inquiry* 1995;32:56–74.
 26. Borghede G, Sullivan M. Measurement of quality of life in localized prostatic cancer patients treated with radiotherapy: Development of a prostate cancer-specific module supplementing the EORTC QLQ-C30. *Qual Life Res* 1996;5:212–222.
 27. Osoba D, Bezjak A, Brundage M, *et al.* Analysis and interpretation of health-related quality-of-life data from clinical trials: Basic approach of the National Cancer Institute of Canada Clinical Trials Group. *Eur J Cancer* 2005;41:280–287.
 28. van Andel G, Bottomley A, Fossa SD, *et al.* An international field study of the EORTC QLQ-PR25: A questionnaire for assessing the health-related quality of life of patients with prostate cancer. *Eur J Cancer* 2008;44:2418–2424.
 29. Talcott JA, Clark JA, Stark PC, *et al.* Long-term treatment related complications of brachytherapy for early prostate cancer: A survey of patients previously treated. *J Urol* 2001;166:494–499.
 30. Merrick GS, Butler WM, Wallner KE, *et al.* Long-term rectal function after permanent prostate brachytherapy. *Cancer J* 2007;13:95–104.
 31. Stock RG, Stone NN, Iannuzzi C. Sexual potency following interactive ultrasound-guided brachytherapy for prostate cancer. *Int J Radiat Oncol Biol Phys* 1996;35:267–272.
 32. Potters L, Torre T, Fearn PA, *et al.* Potency after permanent prostate brachytherapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys* 2001;50:1235–1242.
 33. de Graeff A, de Leeuw JR, Ros WJ, *et al.* Long-term quality of life of patients with head and neck cancer. *Laryngoscope* 2000;110:98–106.