Acute Side Effects after Dose-Escalation Treatment of Prostate Cancer Using the New Urethral Catheter BeamCath® Technique

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Acute side effects after dose-escalated radiotherapy for prostate cancer with different treatment techniques were evaluated, using a daily diary recorded by the patients. Dose escalation was performed using the urethral catheter BeamCath® technique. Side effects were evaluated in 267 patients by means of a daily diary during the treatment and at 3-months' follow-up. The patients' evaluations were compared with those of patients treated with conventional or conformal techniques. Looser stools were reported in the conventional (placebo) and 76 Gy groups at 3-months' follow-up compared with at week 1. No other obvious increase in rectal or bladder morbidity was seen in the 76 Gy group. The catheter did not increase the urinary frequency in comparison to the other groups. The reported urgency and starting problems at the beginning of treatment seemed to improve in all groups at 3-months' follow-up. External beam radiotherapy dose escalation using the BeamCath® technique did not result in a dose-dependent increase in acute side effects.

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External beam radiotherapy has been used as the standard treatment for prostate cancer (PC) for over 35 years. During the late 1980s and early 90s, technical improvement such as three-dimensional conformal radiotherapy (3D-CRT) for PC was accomplished. With the 3D-CRT technique, many authors have reported a decrease in side effects using conformal radiotherapy as compared with the conventional 4-field box technique (1–3). Soffen et al. reported fewer symptoms requiring medication in PC patients treated with conformal radiotherapy in comparison with the conventional technique (4). Further refinement of the 3D-CRT technique has now taken place, with non-axial treatment fields and different kinds of sophisticated intensity-modulated dose distributions (5, 6). A high percentage of patients (40–60%) have biopsy-proven tumor cells remaining in the prostate two years after conventional external beam dose levels (< 70 Gy) (7–10), as well as after brachytherapy (11, 12), which suggests that higher doses are warranted. Refined techniques have been used for dose escalation in an attempt completely to eradicate all prostate tumor cells. Many centers of excellence in the USA are presently performing dose-escalation studies up to and above 80 Gy (13–15). In Europe dose-escalation studies have started in Sweden (Umeå, present article), and randomized trials are under way in Holland (Rotterdam/Amsterdam) and England (London).

Early evaluations of acute side effects after dose-escalation studies show that few side effects have been reported (5, 16) and that a longer follow-up has confirmed that the low acute side effects are accompanied by acceptable late toxicity despite dose escalation (13, 15, 17). Others have also shown that low acute morbidity mostly results in a decrease in late complications (2, 18).

We have recently developed a new stereotactic radiotherapy technique for PC (high precision conformal radiotherapy; HPCRT) using a special urethral catheter containing markers (BeamCath®) that can visualize the prostatic urethra with portal imaging to facilitate correct localization of the prostate prior to treatment (19). This technique makes it possible to adjust the alignment of the beam according to the actual position of the prostate, which can vary by up to 1 cm, depending on factors such as pelvis muscle tension and the degree of bladder and rectal filling (20–22).

Acute side effects are prospectively evaluated daily by means of a self-assessment diary, among the first 91 PC

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Table 1

T-stage and (PSA) values in the different patient groups at the time of diagnosis

T-stage *	Conventional		Conformal	HPCRT	
	Placebo n = 29	Sucralfate n = 27	n = 120	74 Gy n = 27	76 Gy n = 64
T1a			3.3%	7.4%	3.1%
T1b	7% **	4% **	8.3%	3.7%	0%
T1c			2.5%	33.3%	9.4%
T2	59%	63%	50.8%	51.9%	35.9%
T3	28%	30%	25.0%	3.7%	50.0%
T4	6%	3%	10.0%	0%	1.6%
PSA	Placebo ***	Sucralfate ***	n = 94 ****	74 Gy n = 25	76 Gy n = 60
< 10 ng/ml			24.5%	48.0%	20.0%
10–19 ng/ml			25.5%	44.0%	30.0%
20–50 ng/ml			36.2%	8.0%	36.7%
> 50 ng/ml			13.8%	0%	13.3%

* T-stage according to UICC (1992).
** Transformed from T0 according to UICC (1978) to T1b according to UICC (1992).
*** No PSA values were available in these patient groups.
**** PSA values are not available in 26 patients.

patients treated with dose escalation and the new HPCRT technique. These patients are compared with patients previously treated with a conventional 4-field box technique or a conformal technique.

MATERIAL AND METHODS

Patients

This is a prospective community-based, dose-escalation study. All consecutive patients with localized prostate cancer (LPC) referred to the Department of Oncology in Umeå from the northern region of Sweden (800 000 inhabitants) after the 1st of January 1997 were offered the opportunity to participate. The patients included in the study had cytologically or histologically verified LPC. Each patient underwent a clinical examination and blood test (including PSA). Bone scans and pulmonary x-rays were also performed to determine that there was no metastatic spread. A staging operation, routinely via the extra peritoneal approach, was performed on most of the patients for histological examination of pelvic lymph nodes. The patients' T-stage (UICC 1992) and PSA at the time of diagnosis are presented in Table 1.

Instrument

The daily diary contains 14 questions, in two parts: urinary and intestinal function (Appendix). Six questions have straightforward frequencies:

1. Urinary frequency during day
2. Urinary frequency during night
3. Stool frequency during day
4. Stool frequency during night
5. Use of Loperamid
6. Use of Emepron

Five questions have 4-graded verbal answer alternatives ('No', 'A little', 'Quite a bit', and 'Very much'):

7. Starting problems while urinating
8. Urgency
9. Pain while urinating
10. Abdominal cramps

Three questions have 'Yes' or 'No' as answer alternatives:

11. Hematuria
12. Mucus
13. Blood in the stools

One question has 'Water', 'Loose', 'Normal' and 'Hard' as answer alternatives:

14. Stool consistency

Evaluation

The patients started with the daily diary on day one of treatment and continued for 12 weeks (8 weeks in the conventional group). A new daily diary was sent out at 3-months' follow-up after radiotherapy. In this diary, the patients were asked to record their intestinal and urinary functions during a 2-week period. This diary was mailed back to the coordinating nurse and the data were fed into a computer. All patients were given the same daily diary (23) and instructed to report on daily urinary and intestinal functions. Patients treated with the conventional 4-field box technique (placebo or sucralfate) and the first 16 patients treated with the conformal technique used a daily diary that did not contain any questions about urinary function. The daily reported values were summarized to obtain weekly mean values.

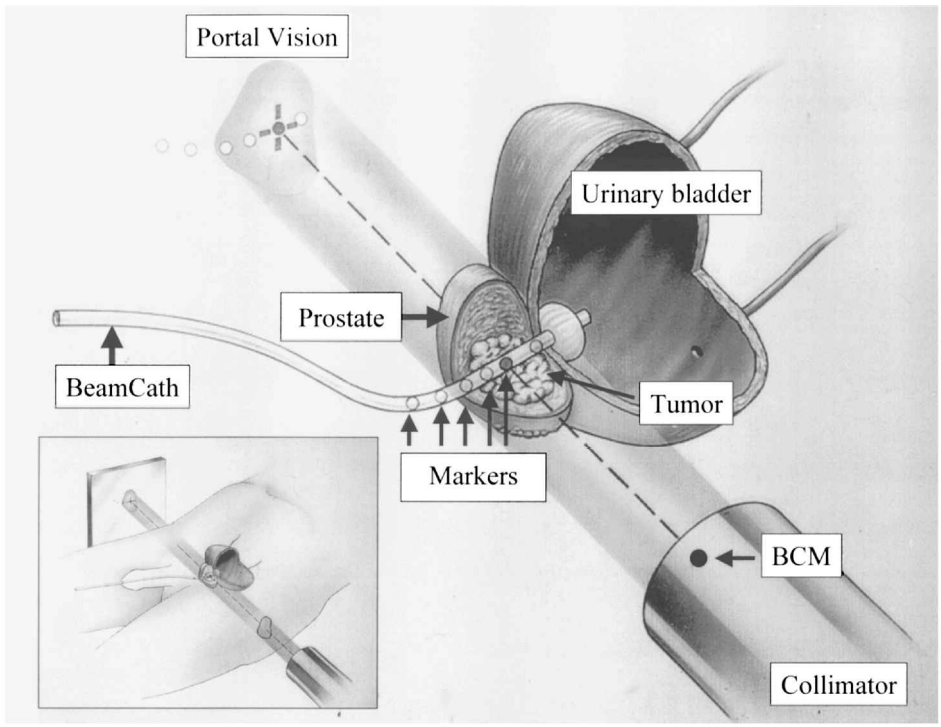

Fig. 1. Principle of the HPCRT technique during treatment. The beam center marker (BCM) placed in the collimator to mark the field center; the catheter in place within the prostate, and the co-localization of the BCM/field center visualized on portal image/film.

In the present study only patients who had completed the questionnaires at all three follow-up times (week 1, week 5 and 3 months) were included.

Treatment technique

All patients were given 5 fractions per week, with a daily dose of 2.0 Gy to a representative point according to the ICRU Report 50 (24). Treatments using the conventional and conformal techniques were given with 20 or 50 MV photons (Racetrack Microtron, Scanditronix, Uppsala Sweden). Patients in the dose-escalation group (HPCRT) were treated on a Varian Clinac 2300C/D, 20 MV with the support of Varian Portal Vision.

In the present study, the side effects of the three treatment techniques in the following four patient groups were compared.

Conventional

Placebo or sucralfate. Between 1986 and 1989, 70 patients were included in a double-blind, prospective, randomized study to compare the effects of placebo and sucralfate during treatment (23). The patients were treated with a conventional 4-field box technique, including the pelvic region. The study also included 7 patients with bladder carcinoma, but they are excluded from this report. Seven patients were not assessable for side effects because they did not have a diary at the start of treatment or at 3-months' follow-up. The remaining 56 patients who reported their side effects in the daily diary are included in this study. The treatment technique in these patients included the pelvic area, to 50 Gy, and then a shrinking field, to a total mean dose of 63.6 Gy to the prostate.

Conformal

Between 1992 and 1996, 120 patients were treated with 64–70 Gy, mainly using a conformal technique. During 1992, approximately 20 patients were treated with the 4-field small box technique, with blocks. From 1993, after the installation of a 3-D dose-planning system (Helax^{TMS}, Uppsala, Sweden), the treatment technique was changed in our department, from the conventional 4-field small box technique, to the 4-field 3D conformal radiotherapy. The CT-based 3D-CRT technique incorporated multileaf collimators or cast conformal blocks. The planning target volume (PTV) in most patients included the prostate, with a 1.5–2 cm margin. Very few patients received treatment to the seminal vesicles. The mean total dose for the conformal therapy group was 65.8 Gy.

HPCRT—high precision conformal radiotherapy

From January 1997 a newly developed technique for dose escalation was used, comprising a special urethral catheter (BeamCath®; patent pending) containing high-density fiducial markers. These markers, indicating the urethra, can be visualized on the treatment machine, for accurate positioning of the prostate (Fig. 1). The catheter is used in

each step throughout the treatment planning procedure. The isocenter is placed on one of the markers, or the most dorsal part of the urethra. On the treatment couch, the markers are visualized on port films or with portal imaging, immediately before dose delivery. A beam center marker (BCM) on the accelerator (collimator) makes it possible to adjust the isocenter position within 1 mm, giving a very high precision, independent of external fixation. The technique involves a simple patient set-up (19). In the dose-escalation study, patients were treated with 74 Gy (T2) or 76 Gy (T3; Table 1). The dose-escalation procedure using the HPCRT technique with BeamCath® was performed as a primary boost for 2–3 treatments with 2 Gy/fractions, at the beginning of the treatment. The PTV included the prostate only, with just enough of a margin to envelop the prostate with the 90% isodose. The rectum was totally shielded. The primary boost was followed by 2 fractions with a PTV margin around the prostate of 1 cm. Thereafter, the PTV included a 1.5–2 cm margin and in T3 tumors the seminal vesicles were treated with 50 Gy. Mean total doses for the two HPCRT therapy groups were 74 Gy and 76 Gy, respectively.

The patients gave their informed consent to participate in the study and the local ethics committee approved the study.

Statistical methods

The 'frequency' variables (see instrument) are reported as median values. The other values are described as the proportion of patients reporting the different levels of problems/function. To evaluate differences between the patient groups, the non-parametric Kruskal-Wallis and Mann-Whitney tests were used. The Wilcoxon matched-pairs signed test was used to calculate the change between the three different time periods (week 1, week 5 and 3 months). Correlation coefficients were calculated according to Pearson and considered significant when $p < 0.05$.

RESULTS

Intestinal symptoms

Stool frequency. An increase in stool frequency per 24 h was seen in all groups as compared with the first week (week 1) and 5 weeks after the start of treatment (Fig. 2). A decrease in stool frequency was noted at 3 months compared with the 5-week evaluation. However, with the exception of the 74 Gy group, stool frequency was still increased in all groups at the 3-months' follow-up in comparison with frequency in the first week. At the 3-months' follow-up, the sucralfate group showed a lower stool frequency than the other groups, except when compared with the 74 Gy group. Patients in the HPCRT groups showed a similar increase in stool frequency as those treated with the conformal technique, despite larger fields, including the seminal vesicles (Fig. 2).

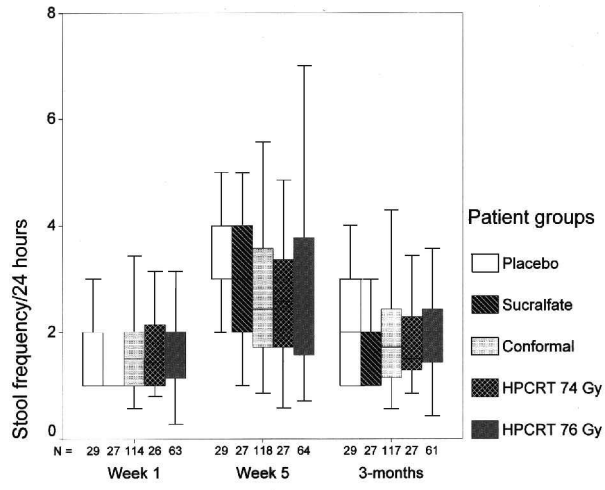

Fig. 2. Stool frequency per 24 h at the start (week 1), during treatment (week 5) and at 3-months' follow-up after radiotherapy in conventional (placebo or sucralfate; 64 Gy), conformal (< 71 Gy) HPCRT-74 Gy and HPCRT-76 Gy groups. Box plots indicate the 25th percentile, median, and the 75th percentile.

Consistency. The conformal and HPCRT groups reported looser stools (not significant) at the start of treatment (Fig. 3). All groups, except the HPCRT-74 Gy group, reported looser stools during radiotherapy (week 5) in comparison to week 1. At 3-months' follow-up, 96% of the patients in the sucralfate group had normal consistency, while 45% of the patients in the conformal and both HPCRT groups (74 Gy = 35% and 76 Gy = 45%) still reported loose consistency (Fig. 3). Looser stools were only reported in the placebo ($p = 0.046$) and 76 Gy groups ($p < 0.000$) at the 3-months' follow-up in comparison to week 1. The HPCRT-76 Gy group reported looser stools at 3-months' follow-up in comparison to the placebo ($p < 0.000$) and sucralfate ($p < 0.000$) groups. This was probably due to the inclusion of seminal vesicles in the HPCRT-76 Gy group.

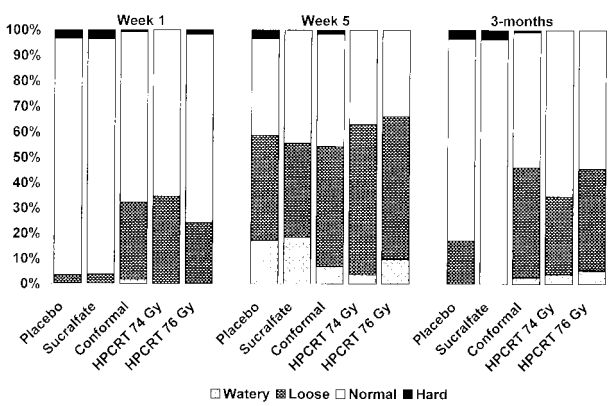

Fig. 3. Stool consistency at the start (week 1), during treatment (week 5) and at 3-months' follow-up after radiotherapy in conventional (placebo or sucralfate; 64 Gy), conformal (< 71 Gy) HPCRT-74 Gy and HPCRT-76 Gy groups.

Table 2

The proportion of patients with occurrence of mucus, intestinal blood and hematuria at start (week 1), during (week 5) and 3 months after the treatment

Symptom	Time	Treatment technique					
		Conventional		Conformal	HPCRT		
		Placebo (n = 29)	Sucralfate (n = 27)	< 71 Gy (n = 120)	74 Gy (n = 27)	76 Gy (n = 64)	p-value *
Occurrence of mucus	Week 1	0%	0%	3%	4%	3%	0.051
	Week 5	55%	44%	31%	37%	41%	0.252
	3 months	17%	7%	21%	19%	20%	0.072
Occurrence of intestinal blood	Week 1	0%	0%	3%	0%	3%	0.097
	Week 5	3%	11%	9%	4%	5%	0.248
	3 months	0%	0%	3%	8%	3%	0.258
Occurrence of hematuria	Week 1	**	**	1%	4%	6%	0.017
	Week 5	**	**	2%	0%	0%	0.804
	3 months	**	**	1%	0%	0%	0.630

* Kruskall-Wallis test.
** The daily diary did not contain this question in these patient groups.

Mucus. All groups reported an increase in mucus during treatment (week 5), but no significant difference could be seen between the groups (Table 2). The sucralfate group reported the lowest frequency of mucus at 3-months' follow-up (7%), while 7–21% of the other groups reported mucus in their stools (Table 2). However, this difference between the conformal and HPCRT groups at the 3-months' follow-up was not significant, despite a higher dose and larger fields in the HPCRT-76 Gy group.

Intestinal blood. Dose escalation with the HPCRT technique did not induce any increase in number of patients reporting blood in the stools in the HPCRT 74 or 76 Gy groups in comparison with the conventional or conformal groups (Table 2). However, the conformal and both of the HPCRT groups reported an increase in intestinal blood when comparing week 1 and week 5 values. The reported level of intestinal blood was normalized to the first week values at the 3-months' follow-up in the conformal and two HPCRT groups.

Intestinal pain. No significant difference between the HPCRT and the other patient groups was reported for intestinal pain at the 3-months' follow-up (Fig. 4). At week 1, patients treated with the conformal and HPCRT technique reported more intestinal pain than the placebo/sucralfate group. No difference was seen between the groups during radiotherapy (week 5). At the 3-month's follow-up, the conformal group reported more problems than both the placebo/sucralfate groups. Comparing the first week and the 3-month values, only the conformal group reported a significant increase in intestinal pain ($p = 0.008$).

Urinary symptoms

Patients treated with the conventional 4-field box technique (placebo/sucralfate) used a daily diary that did not contain any questions about urinary function.

Urinary frequency. Use of the catheter (BeamCath®) in the 74 Gy and 76 Gy groups did not increase the urinary frequency, as compared with the conformal group during the first week of treatment (Fig. 5). As expected, the urinary frequency/24 h, increased during treatment (week 5) in all three groups. The urinary frequency at the 3-months' follow-up was comparable in all groups, to the level in the first treatment week (Fig. 5). No negative influence of dose escalation on urinary frequency using the BeamCath® could be detected despite higher doses and the use of the catheter during the first 2–3 treatments.

Urgency. The HPCRT-76 Gy group had more problems with urgency during the first week of treatment than patients in the conformal group ($p = 0.029$). However, the HPCRT group had more advanced T-stages (Table 1). An

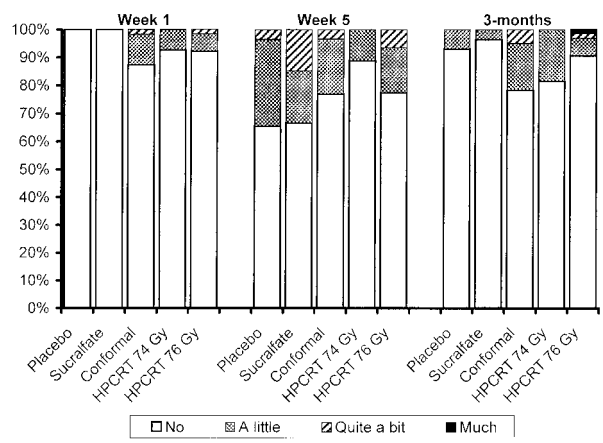

Fig. 4. Intestinal pain at the start (week 1), during treatment (week 5) and at 3-months' follow-up after radiotherapy in conventional (placebo or sucralfate; 64 Gy), conformal (< 71 Gy) HPCRT-74 Gy and HPCRT-76 Gy groups.

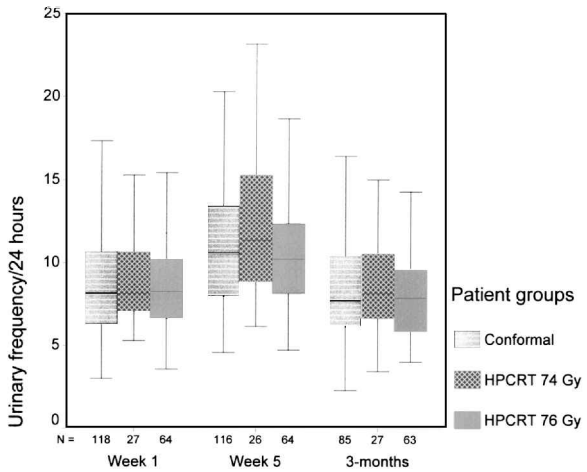

Fig. 5. Urinary frequency per 24 h at the start (week 1), during treatment (week 5) and at 3-months' follow-up after radiotherapy, conformal (< 71 Gy) HPCRT-74 Gy and HPCRT-76 Gy groups. Box plots indicate the 25th percentile, median, and the 75th percentile.

increase in urgency was seen in all groups during radiotherapy (week 5, Table 3). By the 3-months' follow-up, urgency had not only decreased but had actually improved in both the conformal and the 76 Gy groups in comparison with week 1 values (Table 3). The initial difference between the conformal group and the 76 Gy group was not seen at the 3-month follow-up.

Starting problems. The HPRCT-76 Gy group also reported more starting problems than the conformal group in the first week of treatment. In all three groups starting problems increased during treatment. At 3-months' follow-up, fewer problems were seen in comparison with week 1 (Table 3) in both the conformal ($p < 0.000$) and the 76 Gy group ($p = 0.002$). No significant differences could be detected between the three groups at 3-months' follow-up.

Hematuria. Hematuria was not reported as a problem, since only 1%, 4% and 6% in the conformal, HPCRT-74 Gy and HPCRT-76 Gy groups, respectively, reported hematuria at week 1 (Table 2). At 3-months' follow-up, only one patient in the conformal group reported macroscopic hematuria.

Urinary pain. The 76 Gy patient group reported more problems with urinary pain in the first week of treatment in comparison with the conformal group ($p = 0.007$). As expected, urinary pain increased in all three groups during radiotherapy (week 1 to week 5). No significant differences between groups were seen regarding urinary pain at the 3-months' follow-up (Table 3). By the 3-months' follow-up, the level of urinary pain had decreased to similar values as those reported in week 1 (Table 3).

DISCUSSION

The new positioning technique (HPCRT) with a urethral catheter fiducial system (19) has made it possible to increase the total dose up to 76 Gy without increasing acute side effects in comparison with conformal therapy, with doses < 71 Gy. The technique is easy to use in clinical routine and could be used in most patients, without problems.

In a randomized study of conventional versus conformal radiotherapy of pelvic malignancies (prostate 52%; bladder 42%), Tait et al. (22) evaluated acute toxicity with a patient questionnaire using the Lickert scale. No significant differences were seen in acute toxicity. However, a large increase in toxicity was needed in order to detect differences, since increased bowel motion was defined as an 'increase, at any time point, of at least 2 in 24 h, compared to baseline frequency'. An increase in micturition ions was defined as an 'increase in frequency of at least 4 in 24 h, compared to baseline'. The reasons for not detecting the increased acute toxicity seen by others (2) could be the use of scales with different sensitivity, or the moderate difference in normal tissue high-dose volume (689 cm^3 for the conformal technique versus 792 cm^3 for the conventional technique). Nevertheless, there is a trend at 3-months' follow-up toward both bowel motion and micturition frequency to be almost doubled (micturition $p = 0.06$) in the conventional arm as compared with the conformal arm. Comparable toxicity data with extended follow-up of PC patients has only recently been reported (3). In that study the advantage of conformal radiotherapy was clearly shown, with decreased late radiation-induced proctitis. Interestingly, in the questionnaire used in their study (22), Tait et al. showed very similar starting values on number of bowel movements/24 h and micturition/24 h as those reported in the daily diaries in the present study, regarding conformal and HPCRT patients.

A retrospective comparison by Soffen et al. (4), showed that in patients treated with conventional versus 3D-CRT up to 68 Gy, the percentage of patients with urinary and rectal symptoms was similar, although fewer patients treated with 3D-CRT needed bowel medication. Symptom duration also showed a decreasing trend in the 3D-CRT group. A non-randomized study comparing conventional versus CT-based manual versus a beam's eye view-based technique showed significantly lower GU and GI acute toxicity during treatment (7 weeks) in the conformal beam's eye view group (1). All these data clearly demonstrate decreased toxicity for PC using conformal radiotherapy compared with the conventional box technique.

Patients treated with modern conformal radiotherapy and HPCRT-76 Gy reported a lower stool frequency during treatment (week 5) than patients treated with the 'old' 4-field box technique without sucralfate (23) (Fig. 2). A similar result was seen in a previous analysis using the same questionnaire, comparing large box fields and a smaller population of the conformal group (2).

In the group treated with HPCRT-76 Gy, the trend was to report looser stools at 3-months' follow-up in compari-

Table 3

The proportion of patient evaluated levels of urgency, starting problems, and urinary pain at start (week 1), during (week 5) and 3-months after the treatment

Symptom	Time	Treatment technique												
		Conformal 71 Gy (n = 120)				HPCRT 74 Gy (n = 27)				HPCRT 76 Gy (n = 64)				
		No	A little	Quite a bit	Much	No	A little	Quite a bit	Much	No	A little	Quite a bit	Much	p-value *
Urgency	Week 1	64%	21%	13%	3%	52%	30%	15%	4%	45%	38%	14%	3%	0.084
	Week 5	32%	34%	27%	7%	26%	44%	22%	7%	28%	30%	33%	9%	0.583
	3 months	72%	21%	5%	2%	74%	19%	4%	4%	70%	24%	6%	0%	0.416
Starting problems	Week 1	62%	22%	14%	2%	56%	37%	4%	4%	47%	38%	11%	5%	0.118
	Week 5	42%	32%	19%	7%	37%	30%	26%	7%	30%	34%	22%	14%	0.238
	3 months	79%	15%	3%	2%	78%	19%	4%	0%	70%	25%	3%	2%	0.153
Urinary pain	Week 1	80%	12%	7%	1%	89%	4%	4%	4%	70%	23%	5%	2%	0.017
	Week 5	51%	27%	18%	4%	52%	37%	7%	4%	48%	28%	16%	8%	0.878
	3 months	81%	16%	1%	2%	89%	11%	0%	0%	78%	18%	3%	2%	0.515

* Kruskall-Wallis t-test.

son with both the placebo and sucralfate groups. This is probably due to a larger volume of the rectum being treated to 50 Gy because of inclusion of the seminal vesicles in the HPCRT-76 Gy group. This trend was not seen at all in the HPCRT-74 Gy group, which supports previous findings that the volume of rectum treated to high doses correlates with increased rectal toxicity (3, 25). There was clearly an increase in the occurrence of mucus during treatment, but this improved at 3-months' follow-up, although it did not normalize to the starting values of week 1. With a longer follow-up (1 year), 50% of patients treated with the large 4-field box technique will report mucus, as opposed to only 10% of patients in the conformal group (2) and the two HPCRT groups (own unpublished results).

Previously, we have also shown that treatment with the large 4-field box technique carries a higher risk of an increased diarrhea score (2). The protective mucosal effect of sucralfate during radiotherapy of large pelvic fields (23) suggests the use of this drug also in dose-escalation radiotherapy of prostate cancer to improve stool consistency and decrease mucus after radiotherapy, but further analyses are needed.

The University of Michigan (26) was one of the first centers to report on the side effects after dose escalation. Minimal acute toxicity was shown, despite doses of 76 Gy or above. In the randomized study by Pollack et al. (27) comparing conventional radiotherapy up to 70 Gy with 3D-CRT up to 78 Gy, treatment plans revealed that the rectal volume treated above 60 Gy was similar, while significantly less bladder received high doses over 60 Gy. Acute toxicity was almost identical in both arms despite 78 Gy in the 3D-CRT group. Lee et al. (28), using a conventional 4-field box technique and keeping standard margins at 1.5 cm, reported unacceptably high toxicity to the rectum, with RTOG grade II morbidity, in 46 out of 257 patients (18%) after treatment with up to 78 Gy. Lee et al.'s study showed a significant dose response regarding complications, provided the volume of treated normal tissue was not decreased. Using a rectal block, these side effects were significantly reduced to an acceptable 7% late toxicity. Acute side effects in 121 patients treated at MSKCC in their dose-escalation study using conformal radiotherapy with an intensity-modulated technique have been reported (5, 29). The overall incidence of RTOG grade II acute GI toxicity was 16%, and the incidence of acute RTOG grade II GU toxicity was 34%. The trend towards a higher incidence of GU toxicity was especially noted among patients receiving 81 Gy compared with those receiving 75.6 Gy (44% vs. 28%)

Contrary to the increased toxicity reported on above, in our prospective evaluation using patients' daily diaries, we have not been able to detect any increase in acute toxicity when performing dose escalation to 76 Gy using the HPCRT technique with BeamCath® compared with the conformal technique < 71 Gy, using smaller fields. The reason for this could be the very exact localization of the target during dose escalation and the possibility to compensate for variation in target position due to prostate movement (19). Some differences in side effects could also be due to the time point when the evaluation was performed.

As expected, urinary frequency increased during treatment. At 3-months' follow-up the urinary frequency had decreased to the same values as those reported during the first week of treatment, in both the conformal and the HPCRT groups. Tait et al. (22) recorded numbers

for micturition at the start of treatment in their conformal (9.6/24 h) and conventional groups (9.0/24 h) almost identical to those that we found in the present study (8.7/24 h, 9.3/24 h, 8.8/24 h in the conformal group and 74 Gy and 76 Gy in the HPCRT groups, respectively). Of note is that using the catheter along with the HPCRT technique did not increase urinary frequency during the first week in comparison with either the Tait study (22) or the conformal group in the present study. However, the micturition frequency remained on a higher level at 3-months' follow-up in the Tait study, especially in the conventional group (11.0/24 h), while returning to starting levels in the present study (8.7/24 h in the conformal group and 8.2–8.4 in the HPCRT groups). The higher micturition frequency could be explained by the large number of bladder cancers included in the first evaluation Tait study, since the extended follow-up of PC patients only did not report any difference in bladder toxicity, when comparing conformal and conventional toxicity (3).

The improvement of urgency and starting problems 3 months after RT is interesting, since in patients with these problems at the start of the treatment, RT often exacerbates the symptoms during ongoing treatment (Table 3). However, despite the increase during therapy, the present study shows a decrease of these problems at 3-months' follow-up, compared with values at week 1, for both urgency and starting problems. A possible reason for the improvement in symptoms could be a therapy-induced shrinkage of the prostate, which could decrease obstructive symptoms. Since some of the patients had received neoadjuvant hormonal therapy, this might also haveinfluenced the results. This needs further evaluation. As expected, the present study indicates that, as early as the first week of treatment, patients with larger tumors in the HPCRT-76 Gy group (50% T3) have more urgency and starting problems than patients with smaller tumors (conformal = 25% T3). However, these patients (76 Gy) also report improved function at 3-months' follow-up after RT and differences between the groups could no longer be detected.

CONCLUSION

To perform accurate positioning and dose escalation in clinical routine we have used the HPCRT technique with BeamCath®. Despite higher doses (74–76 Gy), and including the seminal vesicles in patients with larger tumors, acceptable levels of patient-evaluated acute intestinal and urinary side effects were detected in comparison to treatment with conventional or conformal RT with lower doses ($<$ 71 Gy). Further dose escalation above 76 Gy seems possible using the HPCRT technique, but a longer follow-up is essential in order to evaluate late side effects.

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APPENDIX

URINARY FUNCTION

Daily Diary

Date / / / / / / /
Number of urinations during the day
Number of urinations during the night
Starting problems while urinating No = 0 A little = 1 Quite a bit = 2 Very much = 3
Urgency while urinating No = 0 A little = 1 Quite a bit = 2 Very much = 3
Pain while urinating No = 0 A little = 1 Quite a bit = 2 Very much = 3
Urinary blood while urinating No = 0 Yes = 1
Fill in how many **Emepron** tablets you have taken during the day. If none, write 0 (zero)

INTESTINAL FUNCTION

Daily Diary

Date / / / / / / /
Number of stools during the day
Number of stools during the night
Starting consistency Watery = 1 Loose = 2 Normal = 3 Hard = 4
Mucus in the stools No = 0 Yes = 1
Blood in the stools No = 0 Yes = 1
Have you had any abdominal cramp? No = 0 A little = 1 Quite a bit = 2 Very much = 3
How many **Loperamid** tablets have you taken during the day. If none, write 0 (zero)