Bladder and Rectal Toxicity of BeamCath® Application in Radiotherapy of Prostate Cancer

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Abstract. *Background: Patient-reported toxicity in two radiotherapy regimens for early stage prostate cancer was investigated. In 2003, the Swedish BeamCath® technique was adapted for Northern Norway. Materials and Methods: Ninety men underwent radiotherapy for early-stage prostate cancer in February 2002 to March 2005. They were invited to participate in a telephone interview employing a questionnaire guide focusing on bladder, intestinal and sexual function. Results: Eighty patients responded, which represents 89% of all patients. The treatment group (23 patients) had received 76 Gy with the BeamCath® technique and the control group (57 patients) received 70 Gy employing a conformal technique. The BeamCath® technique was associated with a lower median rectal (p=0.004; 50.6 Gy versus 56.2 Gy) and bladder dose (p=0.017; 48.5 Gy versus 61.5 Gy). There were no differences in scores on masculinity and sexual function. In conclusion, the BeamCath® technique did not increase rectal or bladder toxicity.*

Prostate cancer is the commonest cancer among Norwegian men and its incidence has increased by 55% during the last decade (1). The majority of patients (73%) are above 65 years. The relative risk (RR) of prostate cancer is lowest (RR <0.62) in northern and highest (RR 1.58) in southern Norway (1). The Scandinavian countries have among the highest incidence and mortality rates observed, and Norway has the highest reported mortality rate worldwide (1-3).

The increased risk of prostate cancer requires improved methods for surgery, radiotherapy, endocrine treatment and combined therapy. In radiotherapy, a major American study focused on three dose levels (≤67, >67-77, >77 Gy) and revealed disease-free survival (DFS) improving with total dose (4). A similar study (5) documented an improved cure rate when the total dose was raised from 70 to 78 Gy. Intermediate- and high-risk patients frequently experienced relapse when the total dose was 70 Gy or less (5). However, higher doses are known to introduce more acute and late toxic effects, especially affecting the rectum and bladder.

In January 1997, a new technique was launched in Umeå in Sweden (6-9). In this study, we document our experience with this technique compared with the prior standard employed.

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Materials and Methods

The main objective of this study was to clarify the effects of BeamCath® application (6 Gy) combined with conformal technique (70 Gy) *versus* conformal technique (70 Gy) alone on toxicity in radiotherapy in early-stage prostate cancer. The BeamCath® technique employs a specially designed catheter with radio-opaque markers indicating the position of the urethra which is visualised on the linear accelerators (LINACs) portalvision imaging (PVI) system. The catheter thus allows more accurate positioning of the prostate within the irradiated field.

Figure 1 illustrates the principles of the method.

Study population. The study population comprised patients recruited from the Section of Radiotherapy at the Department of Oncology, University Hospital of North Norway (UNN). The patient administrative system: (Verification and Information System in Radiotherapy (VISIR)) was used to select patients according to specific inclusion and exclusion criteria. The patients' addresses were recorded from the hospital's patient administrative system (Distributed Information and Patient data System (DIPS)) and their status as survivors were simultaneously verified.

The following inclusion and exclusion criteria were employed:

- Treatment group (BeamCath® technique): Patients diagnosed with localised prostate cancer (C61, International Classification of Disease (ICD-10)) limited to the prostate gland and treated with the BeamCath® technique from 1 June 2003 to 31 March 2005.
- Control group (conformal technique): Patients with localised prostate cancer treated with conformal technique from 1 January 2002 to 31 March 2005.

The exclusion criteria resulted in omission of patients who: a) had not returned the consent form; b) were not able to handle a telephone call and/or respond to the questions; c) had not followed the treatment plan; d) were not alive at study initiation.

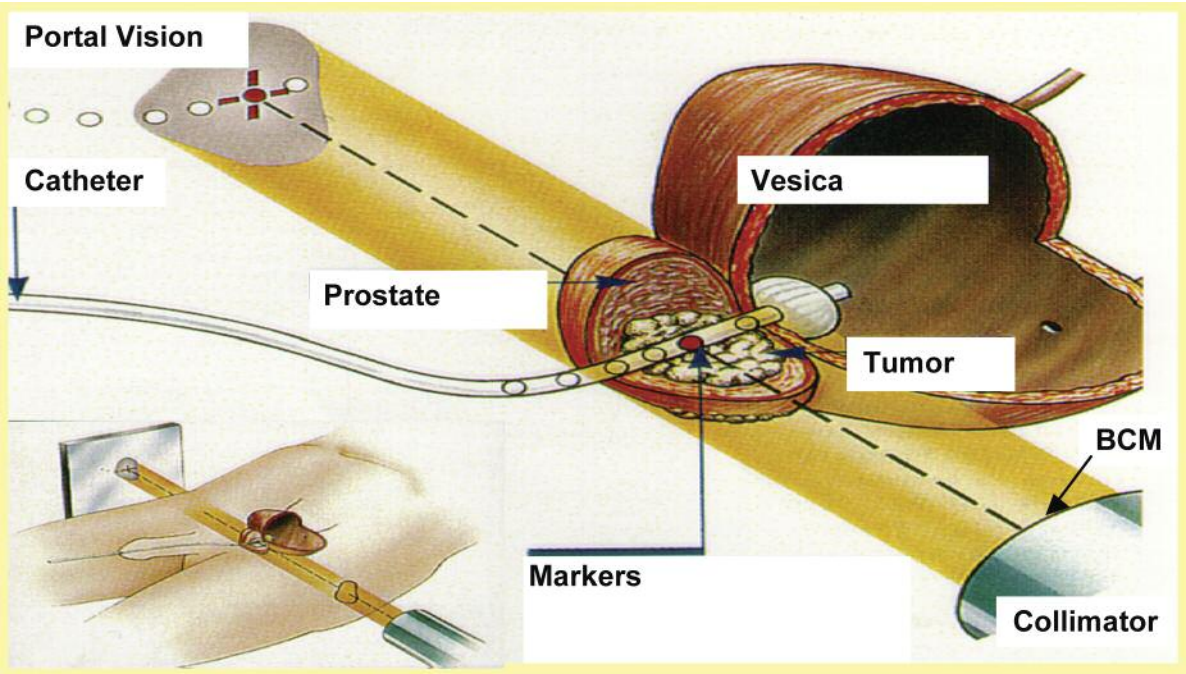

Figure 1. *BeamCath® technique (catheter with markers and balloon) is illustrated, placed in correct position for CT scan, simulation and radiotherapy (13).*

Ninety patients were selected. In order to obtain a 1:2 ratio between the groups, the control group was recruited over a longer time period (17 months). Patients were divided into three risk groups based on prostate specific antigen (PSA) level, grade of primary tumour (T stage) and Gleason score.

Radiotherapy. The treatment group (the BeamCath® group): In patients with intermediate risk (stage T1–T2, PSA 10-20 μg/l, Gleason score <4+3; or stage T1–T2, PSA <20 μg/l, Gleason score <3+4; or T3a, PSA <20 μg/l, Gleason score 4+3) the clinical target volume (CTV) included only the prostate gland for the first three sessions. During the subsequent 35 sessions, the prostate gland was irradiated with margins between 1.0 and 1.5 cm. High-risk (T3a and/or Gleason >=4+3=7, PSA >20 μg/l) patients were treated the same as the intermediate group, but in addition the base of the seminal vesicles received 50 Gy. The control group (conformal treatment): Patients with T1–T2, PSA <10 μg/l and Gleason score <4+3 tumours were registered as the low-risk group and those with T3b tumours were classified as the high-risk group.

A Varian CLINAC 2100 C/D (LINAC), employing 15 MV photon energy was used. All patients received five fractions per week, a daily isocentre dose of 2 Gy, in accordance with The International Commision on Radiation Units and Measurements (ICRU) report 62 (10). Details of the BeamCath® technique have been described elsewhere (6-9).

Questionnaire. Selected questions from the validated international questionnaire of the European Organisation for Research and Treatment of Cancer (EORTC) were used. From the prostate cancer-specific module EORTC QLQ-PR25, question numbers 37 and 49 were selected. In addition, questions 35, 47, 58 and 60 from the Scandinavian Prostate Cancer Group's study (SPCG-7/SFUO-3) were included. Questions were selected to clarify toxic effects on the bladder and rectum.

All patients received a letter including information, the questionnaire, two consent forms and a stamped addressed envelope (28 April to 2 May). A reminder was sent on 26 May. Participants were telephoned two to ten days after the consent form was received and their responses recorded. They were allowed time to talk about problems directly related to the questions and other factors of importance, positive as well as negative.

Statistical analyses and authorisations. Windows Excel 2003 version 11.0 was used for the final database and the Statistical Package for the Social Sciences (SPSS) version 13.0, for statistical analyses. The answer on each question was recorded on a 0-100 scale. [0 (not at all), 33 (a little), 67 (quite a bit) and 100 (very much)]. Patients with an unknown value for a particular variable were excluded from analysis involving that variable.

A significance test between the groups on questions 1-6, and for rectum and bladder doses was carried out. A t-test was used to calculate mean, standard deviation and 95% confidence intervals. One-way ANOVA was used to test significant differences between continuous variables for the two groups. Pearson's correlation coefficient was used to analyse correlations between the questions, and individual correlations between BeamCath® and conformal technique. Logistic (ordinal) regression was carried out to calculate marginal percentage values for questions 1-6.

The project was approved by the Regional Committee for Medical Research Ethics, North Norway (REK Nord) and the Norwegian Social Science Data Services (NSD). EORTC gave authorisation for the use of their questionnaires.

Table I. *Patient characteristics*.

Variable	BeamCath® (N=23) treatment group	Conformal (N=57) control group
Age (years)		
Mean (median)	66.2 (65.7)	65.5 (65.8)
Range	57.4-76.0	54.9-74.9
Treatment period	1 Jun 2003-31 Mar 2005	1 Jan 2002-31 Mar 2005
County of residence		
Nordland	12	24
Troms	8	25
Finnmark	2	7
Other	1	1
Total dose (Gy)	76	70
Number of fractions	38	35

Results

Eighty patients (89%) responded and took part in the study. There were 57 patients in the control group and 23 patients in the treatment group. The mean ages of responders and non-responders were 65.7 and 67.8 years, respectively. The corresponding figures for the treatment group and control group were 66.2 and 65.5 years. Further details are shown in Table I. There was no significant difference between the groups for each of the six questions. Details can be seen in Table II.

A significant correlation between BeamCath® treatment and a lower median rectum dose (p=0.004, 50.6 Gy *versus* 56.2 Gy) was revealed by ANOVA (Table III). The correlation analyses revealed a correlation between the median rectum dose and question 5 (masculinity) (p=0.014) and age above 65 years (p=0.005). Furthermore, we observed a correlation between the BeamCath® technique and the median dose to the bladder (p=0.017, 48.5 Gy *versus* 61.5 Gy). The response to each question is shown in Table II. There were no statistically significant differences, but there was a trend towards more urinary symptoms (question 1) in the BeamCath® group (p=0.09). The frequency of "quite a bit" responses for sexual problems (question 6) was 35% and 21% in the two groups, respectively (p=0.16).

During the telephone interview, patients were given the opportunity to add comments. One quarter (18/80) of the patients reported at least some problems with rectal and/or anal function. This had a constant influence on their social life and three of them did not dare to travel by plane due to risk of incontinence. General comments added were the importance of support from family and friends, exercise to preserve physical fitness and a good sense of humour.

Discussion

In this survey, we have revealed a correlation between the BeamCath® technique and median radiation doses to the rectum and bladder. We have also shown that radiotherapy to the prostate gland is associated with significant toxic effects, but with no statistical difference between the BeamCath® and the control group. This strongly indicates that the dose can safely be escalated employing the BeamCath® technique.

A limited number of epidemiological studies focusing on radiation treatment of prostate cancer have been published.

Table II. *Questionnaire responses according to treatment group, as a percentage of the whole group*.

Question	BeamCath® (N=23) treatment group	Conformal (N=57) control group	p-Value
1. Did you experience any dysfunction from your urinary tract?			
Not at all	21.7	43.9	
A little	43.5	38.6	
Quite a bit	30.4	10.5	
Very much	4.3	7.0	0.09
2. Did you have pain when you urinated?			
Not at all	52.2	56.1	
A little	30.4	35.1	
Quite a bit	13.0	7.0	
Very much	4.3	1.8	0.42
3. Did you have problems with passing stools?			
Not at all	34.8	21.1	
A little	34.8	45.6	
Quite a bit	26.1	21.1	
Very much	4.3	12.3	0.29
4. How much have your stool problems affected your daily life?			
Not at all	60.9	47.4	
A little	21.7	24.6	
Quite a bit	13.0	22.8	
Very much	4.3	5.3	0.28
5. Have you felt less masculine as a result of your illness or treatment?			
Not at all	8.7	3.5	
A little	21.7	29.8	
Quite a bit	43.5	35.1	
Very much	26.1	31.6	0.73
6. Have you experienced problems with your sexual life?			
Not at all	0.0	0.0	
A little	8.7	30.0	
Quite a bit	34.8	21.0	
Very much	56.5	49.0	0.16

Table III. *Dosage to rectum and bladder.*

Variable	BeamCath® treatment group (N=23)	Conformal control group (N=57)
Rectum dose (Gy)		
Median	50.6	56.2
Range	34.0-73.4	40.1-68.7
Vesica dose (Gy)		
Median	48.5	61.5
Range	30.7-71.0	42.0-71.1

The first Scandinavian study using the BeamCath® technique and dose escalation revealed no difference in acute side-effects (6). A prospective study by Fransson *et al*. (8) with a follow-up of one (n=287) and three years (n=153) employed doses of 74, 76 and 78 Gy for the BeamCath® technique (n=195) and an average dose of 66 Gy for the conformal technique (n=168). The highest doses did not increase late side-effects (gastrointestinal or urogenital) compared with doses of 70 Gy or less. This has also been supported by another study, focusing on the conformal technique (n=228) and the BeamCath® alternative (n=104) (9). Our findings are in accordance with the results from these three Swedish surveys.

During the telephone interviews, the importance of family support and interpersonal relationships were underlined. This has also been shown by Owens and colleagues (11). They conclude that families and friends are the most important source of support and encouragement. Several men in our study emphasised the benefit of having contact with other patients in the same situation during treatment and the opportunity to maintain contact following therapy. The benefit of support from other "patient-colleagues" was also described in an English study (11).

We employed only six questions focusing on bladder and rectal toxicity in our survey. It could be argued that we should have used a complete version of the questionnaire and thus achieved a better overview of patients' quality of life. On the other hand, interview by phone is recommended to include a limited number of questions to avoid creating a patient-researcher relationship which may introduce bias (12). To balance this factor, we focused on the two main topics in pelvic irradiation: bladder and rectal toxicity.

This was not a randomised study and the two groups differed in some respects (Table I). The study population comprised only 80 patients and a 1:2 ratio was used, resulting in low statistical power. On the other hand, all patients at this single institution were included. We believe that when treatment regimens are altered, side-effects and patients' quality of life should be investigated. This retrospective study documents that we have achieved our primary goal of reducing the dose to the rectum and bladder, while increasing the total dose by 6 Gy.

In conclusion, this study documents that the BeamCath® technique in early prostate cancer offers a dose escalation from 70 to 76 Gy without affecting bladder and rectal toxicity, and a lowered median dose to these organs can be achieved.

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