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Original Article

# The Effect of High Dose Rate Brachytherapy in Combination with External Beam Radiotherapy on Men's Health-related Quality of Life and Sexual Function over a 2 Year Time Span

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## Abstract

*Aim:* To investigate changes in health-related quality of life and sexual function in men after high dose rate (HDR) brachytherapy and external beam radiotherapy (EBRT), with or without androgen deprivation therapy, for localised prostate cancer.
*Materials and methods:* Eligible men who had undergone HDR brachytherapy/EBRT for their prostate cancer completed questionnaires before any treatment (baseline) and at 3 monthly intervals. The European Organization for Research and Treatment of Cancer (EORTC) C30 quality of life measure (QLQ-C30), the PR25 prostate-specific supplement and the International Index of Erectile Function-Short Form (IIEF-SF) were completed. An analysis of changes from baseline to 2 years, for the 87 men who completed surveys, was carried out.
*Results:* The mean EORTC QLQ-C30 quality of life scores, urinary, bowel and sexual symptoms had all improved. However, improvements did not return men to baseline levels at 2 years. Sexual function as measured by both scales was least likely to recover. There were no differences due to androgen deprivation therapy. Minimally important differences were still reported by men at 2 years as follows: urinary (36%), bowel (24%), hormone treatment side-effects (40%), IIEF-SF (55%). Discrepancies between mean and minimally important differences changes are explained by some men remaining more affected by their therapy than others.
*Conclusion:* The findings do not support our first hypothesis that urinary, bowel and sexual problems in these men will return to baseline levels once therapy is completed and 2 years have elapsed. Our findings indicate the changes men experience are significant, do occur early, and many do not resolve in the longer term.


*Key words:* Androgen deprivation therapy; external beam radiotherapy; high dose rate brachytherapy; prostate cancer; quality of life; sexual function

## Introduction

Prostate cancer is one of the most common cancers in the western world. In New Zealand it was the most commonly registered cancer among men in 2007 (15.1%) [1]. If treatment occurs when cancer is localised, men often survive years, living with the treatment effects on their urinary, bowel and sexual functioning [2]. The increasing numbers of survivors of prostate cancer, and the range of health-related quality of life issues associated with the sequelae of treatments for the cancer, make understanding these consequences crucial for the men faced with choosing between therapy options. Unfortunately, evaluation of the various prostate cancer treatments with respect to health-related quality of life is not conclusive in the literature, so men facing treatment choices, and the clinicians guiding them, have relatively few data on which to base therapy decisions [3].

Radiotherapy represents one of two primary curative treatment modalities for patients with prostate cancer, the other being surgery (radical prostatectomy). This paper focuses on the changes in health-related quality of life that occur as a consequence of high dose rate (HDR)

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brachytherapy in combination with external beam radiotherapy (EBRT), a method of dose escalation with good rates of tumour control [4].

Evidence detailing the outcomes for men receiving HDR brachytherapy/EBRT is still accumulating. One early report concluded that, although brachytherapy was a promising therapy for prostate cancer, and problems were mainly urinary and temporary in nature, the data on impotence were yet to be collected [5]. Egawa *et al.* [5] suggested that quality of life in men receiving HDR brachytherapy/EBRT returned to normal by 1 year and sexual function was not affected. A 2005 review noted significant decreases in sexual function in men undergoing interstitial brachytherapy, with little improvement at a 1 year follow-up [6]. A comparison of radical prostatectomy, permanent low dose radiotherapy, interstitial brachytherapy and HDR brachytherapy found little or no difference in outcomes between treatment modalities, but only reported on a 3 month follow-up [7]. Morton *et al.* [8,9] reported short- and longer-term adverse effects of HDR brachytherapy in intermediate-risk prostate cancer at 2 years of follow-up.

The addition of androgen deprivation therapy (ADT) for cytoreduction before radiotherapy or concurrent/adjuvantly following radiotherapy also potentially affects health-related quality of life. ADT has a significant effect on men's energy, lean body mass, testicular size and libido levels [10]. Health-related quality of life in men receiving ADT has been shown to decrease regardless of the duration of the therapy [11]. The suggestion has been made that ADT might be unnecessary in combination with HDR brachytherapy/EBRT, thus avoiding the negative effects on health-related quality of life in these men [12].

Health-related quality of life outcomes are variously reported as mean values at relevant time points or, more recently, as minimally important differences (MID), the proportion of patients recording a decrement of $>0.5$ standard deviation of baseline score. Reporting the proportion of patients with MID quantifies the clinically significant changes experienced by men during and after treatment for their prostate cancer [8].

In 2006, HDR brachytherapy in combination with EBRT for prostate cancer was introduced into New Zealand at Waikato Hospital. Since then, 196 patients have received this therapy, some in combination with ADT and others without. This paper reports a prospective study of the 2 year outcomes for those men with respect to their health-related quality of life and sexual function.

The aim of the study was to determine health-related quality of life outcomes for men with prostate cancer referred to radiation oncology for HDR brachytherapy/EBRT, including the effect of ADT in those men receiving it.

We assumed two hypotheses: (1) That measures of men's urinary, bowel and sexual symptoms will return to baseline levels at 2 years. (2) That men undergoing ADT in addition to HDR brachytherapy/EBRT will differ significantly in their sexual function, from those not receiving ADT, at 2 years.

## Materials and Methods

### *Patient Recruitment*

This was a single centre study based at a tertiary referral hospital. The regional ethics committee approved the implementation of this technology and the associated data collection. One hundred and ninety-six men, diagnosed with prostate cancer, and referred to the cancer unit for HDR brachytherapy/EBRT between January 2006 and July 2010, consented to be surveyed. The patient's risk category was determined from their prostate-specific antigen level, digital rectal/magnetic resonance imaging examination findings and Gleason's score (as determined on a transrectal ultrasound-guided core biopsy). Patients in this study were either intermediate- or high-risk (defined by D'Amico *et al.*'s criteria [13]). Patients in the intermediate-risk group were offered ADT (6–9 months, for cytoreductive purposes) if their gland size exceeded 50 $cm^3$. Men in the high-risk group had ADT before and concurrent with HDR brachytherapy/EBRT, as well as adjuvant ADT for 1–3 years after the completion of radiotherapy.

### *Treatment Details*

The pre-treatment evaluation included a baseline magnetic resonance imaging scan of the pelvis and an isotope bone scan, uroflowmetry and prostate-specific antigen. The treatment protocol consisted of EBRT (45–46 Gy in 23–25 fractions over 4.5–5 weeks) combined with a boost of HDR brachytherapy (two fractions of 9.5 Gy each – total dose 19 Gy) using $^{192}Ir$, carried out as a single implantation using a trans-perineal approach with transrectal ultrasound guidance. The EBRT and HDR phases of therapy were separated by 1–3 weeks. The position of the needles followed the typical placement pattern. The number of needles inserted ranged between 12 and 21. Each fraction was separated by at least 6 h. The implant was carried out under spinal anaesthetic with default to general anaesthesia if necessary. Dosimetry was optimised post-implant and preceding each fraction, using computer-based three-dimensional planning. The goal was to deliver 9.5 Gy to $>95\%$ of the prostate volume and to limit the doses to critical structures: V125 urethra $<1$ $cm^3$, V150 urethra $= 0$ $cm^3$ and V75 rectum $<1$ $cm^3$. No predefined normal tissue dosimetric constraints were used for EBRT.

### *Data Collection*

Over the 4 year period, 196 men were entered in the database. Questionnaires were mailed to participants at 3 monthly intervals and returned in a prepaid envelope. If participants failed to return a questionnaire they were reminded once, but recorded as not returned after a month. Some 716 questionnaires were returned completed (169 at baseline, the remainder at various other time points). Questionnaires clustered around the 2 year (22–26 months) time point have been collated for comparison with