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*Prostate brachytherapy*

# Novel prostate brachytherapy technique: Improved dosimetric and clinical outcome

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## Abstract

***Purpose*: Erectile dysfunction following prostate brachytherapy is reported to be related to dose received by the penile bulb. To minimise this, whilst preserving prostate dosimetry, we have developed a technique for I-125 seed brachytherapy using both stranded seeds and loose seeds delivered with a Mick applicator, and implanted via the sagittal plane on trans-rectal ultrasound.**

***Materials and methods*: Post-implant dosimetry and potency rates were compared in 120 potent patients. In Group 1, 60 patients were treated using a conventional technique of seeds implanted in a modified-uniform distribution. From January 2005, a novel technique was developed using stranded seeds peripherally and centrally distributed loose seeds implanted via a Mick applicator (Group 2). The latter technique allows greater flexibility when implanting the seeds at the apex. Each patient was prescribed a minimum peripheral dose of 145 Gy. No patients received external beam radiotherapy or hormone treatment. There was no significant difference in age or pre-implant potency score (mean IIEF-5 score 22.4 vs. 22.6, $p = 0.074$) between the two groups.**

***Results*: The new technique delivers lower penile bulb doses ($D_{25}$ as %mPD — Group 1: 61.2 ± 35.7, Group 2: 29.7 ± 16.0, $p < 0.0001$; $D_{50}$ as %mPD — Group 1: 45.8 ± 26.9, Group 2: 21.4 ± 11.7, $p < 0.0001$) whilst improving prostate dosimetry ($D_{90}$ — Group 1: 147 Gy ± 21.1, Group 2: 155 Gy ± 16.7, $p = 0.03$). At 2 years, the potency rate was also improved: Group 1: 61.7%; Group 2: 83.3% ($p = 0.008$).**

***Conclusions*: In this study, the novel brachytherapy technique using both peripheral stranded seeds and central loose seeds delivered via a Mick applicator results in a lower penile bulb dose whilst improving prostate dosimetry, and may achieve higher potency rates.**



*Keywords:* Prostate brachytherapy; Erectile dysfunction; Penile bulb; Implant technique

Prostate brachytherapy continues to be used as a curative treatment option for localised prostate cancer. Biochemical control rates are reported to be excellent and equivalent to those for radical prostatectomy and conformal external beam radiotherapy (EBRT) [1–3]. Thus, when discussing treatment options with the patient, issues such as post-treatment quality of life and sexual function become increasingly important [4–7]. Consequently, the selection of a treatment modality by the patient is often preceded by an extensive evaluation of treatment-related morbidity [8].

Erectile dysfunction (ED) is a common complication of all potentially curative therapies for early prostate cancer [9], and is reported to occur in 6–53% of cases after permanent prostate brachytherapy alone [10–13]. The aetiology of this is not completely understood, but is likely to be related to multiple factors, including issues such as local neurogenic and vascular compromise, as well as psychogenic causes [14]. The structures of the proximal penis, namely the penile bulb and proximal crura, have been implicated as being site-specific structures implicated in the development of ED after brachytherapy [15–17]. Two studies have shown no discernible relationship between radiation dose to the neurovascular bundles and post-treatment loss of erectile function [13,18].

In this study, we have investigated the effect of a novel brachytherapy implant technique, which aims to minimise the radiation dose delivered to the penile bulb. This technique was designed to implant stranded seeds in the peripheral prostate gland, and loose seeds centrally via the Mick applicator. Seeds are implanted under direct visualisation in the sagittal trans-rectal ultrasound plane, which allows for greater precision of seed placement, particularly at the prostatic apex. We have evaluated the effect of this

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technique in terms of radiation dosimetry to the penile bulb and prostate, as well as post-implant potency preservation.

## Materials and methods

At our centre, the I-125 prostate brachytherapy programme began in March 1999. After an initial learning curve [19,20], a total of 120 patients with pre-implant potent erectile function underwent I-125 permanent prostate brachytherapy for clinical stage T1c—T2c prostate cancer (2002 American Joint Committee on Cancer) [21]. Potency was defined using the International Index of Erectile Function-5 (IIEF-5) survey score of $\geqslant$11/25 [22,23].

All the patients underwent a trans-rectal ultrasound-guided two-stage implant. Treatment plans were generated prior to the implant date using Variseed 7.1 planning software (Varian Medical Systems, Inc., Palo Alto, CA, USA), without the subsequent use of intra-operative real-time planning. Patients in Group 1 ($n$ = 60) were treated (non-consecutively) between September 2001 and January 2004 using the classical modified-uniform implant technique, as developed in Seattle [24]. From February 2005, the novel technique was instituted, and 60 patients who underwent this technique were analysed as Group 2. For this technique, stranded seeds (RapidStrand™, Oncura, Plymouth Meeting, PA, USA) were implanted into the peripheral prostate. Following this, loose seeds were implanted more centrally using the Mick applicator through between 4 and 6 needles. All the seeds were delivered under direct vision in the sagittal trans-rectal ultrasound plane to ensure conformity to the prostate gland, particularly at the apex. Fig. 1 demonstrates pre-plan images from the mid-gland and apex, showing needle geometry and isodoses for each implant technique.

No patients received supplemental EBRT or androgen deprivation therapy. All were prescribed a minimal peripheral dose (mPD) of 145 Gy. The mean pre-treatment PSA, Gleason score, clinical stage, prostate volume, age and IIEF-5 scores were similar between the two groups, as shown in Table 1. The median Gleason score was 6 in both group (Group 1: range 3—7; Group 2: range 5—7). In terms of clinical stage, no patients were documented to have clinical or radiological extracapsular disease.

Post-implant CT imaging for dosimetric assessment was performed on day 1 [25,26], with the penile bulb contoured at 5 mm intervals on the CT images. At present, MR imaging is not available as standard practice at our centre for this purpose. The penile bulb was contoured by the authors SJK, MAH and JPN, as trained by an independent Uro-Radiologist. The physicians who contoured the penile bulb were not blinded as to which implant technique the patient underwent. Prostate and penile bulb dosimetry was recorded. Erectile function was evaluated at baseline, 12 and 24 months following treatment using the IIEF-5 score. Phosphodiesterase-5 inhibitor use, which is encouraged in the first year after implantation as part of the overall treatment protocol, was also recorded [27].

Unpaired $t$ tests were used to make statistical comparisons between the demographic, dosimetric and clinical parameters in the two groups. Non-parametric tests were used to assess non-linear data. For all the tests, $p \leqslant 0.05$ was considered statistically significant. Statistical analysis was performed with Minitab version 14.

## Results

Table 2 summarises the penile bulb post-implant dosimetry recorded for each implant technique using day 1 CT-based analysis. All dosimetric parameters were statistically lower using the novel technique. In particular, the $D_{25}$ and $D_{50}$ comply with previously recommended constraints of <60% and <40%mPD, respectively (Group 1 vs. Group 2: 61% vs. 30%; 46% vs. 21%, $p < 0.0001$) [16].

Prostate dosimetry also differed between the groups (Table 3). Prostate implant quality was significantly improved in Group 2 ($D_{90}$ 147 Gy vs. 155 Gy, $p = 0.03$), with a trend to increased dosimetric coverage ($V_{100}$ 90.7% vs. 91.7%, $p = 0.29$). However, this did not result in a simultaneous unfavourable increase in prostate $V_{150}$ (55% vs. 53%, $p = 0.27$).

All the patients completed an IIEF-5 score at baseline and at 12 and 24 months, with a score of $\geqslant$11/25 defining potency. The distribution of IIEF-5 scores pre- and 24 months post-implant is demonstrated in Fig. 2 for both implant techniques. Table 4 illustrates potency preservation post-brachytherapy. There is a significant improvement in potency preservation using the novel technique at 2 years (61.7% vs. 83.3%, $p = 0.008$), with a greater documented use of phosphodiesterase-5 inhibitors in Group 1 (53.3% vs. 31.7%, $p = 0.016$) at this time point. Mean IIEF-5 scorer were higher in Group 2 at 12 months (14.1 vs. 18.0, $p = 0.006$) and at 24 months (12.9 vs. 17.9, $p = 0.001$). The average change in IIEF-5 score between baseline and 24 months post-implant was also significantly lower in Group 2 (−9.5 vs. −4.7, $p = 0.001$). Interestingly, there was little reduction in IIEF-5 score after 1 year (−1.2 vs. −0.07, $p = 0.37$), with 12-month potency rates being similar to those a year later (65% vs. 85%, $p = 0.011$).

## Discussion

Erectile dysfunction is a common sequela of curative therapies for early prostate cancer, and can have an adverse effect on quality of life [9,28]. Although it has been claimed that preservation of erectile function is more likely after brachytherapy, the incidence of brachytherapy-induced ED is actually greater than initially described [29,30]. ED has been demonstrated in subgroup analyses in 6—90% of patients undergoing brachytherapy alone or with additional therapies such as external beam radiotherapy or androgen deprivation therapy [10—13,17,22,30,31]. The wide ranges of reported ED are likely to reflect the use of retrospective analyses, unclear definitions of potency, use of non-validated instruments to assess potency, and studies where a single question regarding erectile function was asked [32]. The rate of ED following prostate brachytherapy will also vary with age, co-morbidities, pre-potency and phosphodiesterase-5 inhibitor use of the study population. There is increasing evidence that brachytherapy-induced ED may also be technique-related and so potentially minimised by precise attention to seed placement [33].

The radiation dose to the prostate gland and its surrounding structures has been studied in order to identify an association with the development of post-implant ED. The largest body of evidence supports the penile bulb and prox-