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# Manual vs. automated implantation of seeds in prostate brachytherapy: Oncologic results from a single-center study

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**ABSTRACT**

**PURPOSE:** The objective of this study was to study survival and tolerance of prostate cancer patients treated with $^{125}$I permanent interstitial brachytherapy by automated vs. manual implantation of seeds.

**METHODS AND MATERIALS:** Between 2002 and 2010, 349 selected patients were treated with $^{125}$I brachytherapy by the same team: from 2002 to April 2005, 65 patients with linked seeds and then 284 patients treated using Nucletron First System automated implantation. We analyzed biochemical recurrence-free survival (bRFS) rates and toxicities (univariate and multivariate analyses).

**RESULTS:** Two hundred seventy-seven (79.4%) and 69 patients (19.8%) with low- and intermediate-risk disease were treated, respectively (median follow-up: 64 months). The 5-year bRFS rate was 93.1% (95% confidence interval 89.3−95.6) for the entire cohort. The 5-year bRFS rates were 93.4% and 91.7% for patients with low- and intermediate-risk disease, respectively ($p = 0.42$). In univariate and multivariate analyses, there was no statistically significant difference in the 5-year bRFS rate depending on the implantation technique (93.1% vs. 91.8%, respectively, for automated and linked seeds; $p = 0.53$). In univariate analysis, only $D_{90}$ prostate (dose delivered to 90% of the prostate) <140 Gy ($p = 0.01$), lack of prostate-specific antigen bounce ($p = 0.008$), and nadir prostate-specific antigen >0.11 ($p = 0.01$) were predictive factors for bRFS. We observed Grade 3 urethritis in 7 patients (2%), urinary incontinence in 2 patients (0.7%), and Grade 4 proctitis in 2 patients (0.7%).

**CONCLUSIONS:** In this large single-center series, brachytherapy for selected localized prostate cancer achieved excellent rates of biochemical control at 5 years (93.1%) with an acceptable toxicity profile, irrespective of the implantation technique used. 

*Keywords:* Prostate cancer; Brachytherapy; $^{125}$I; Automated seed implantation

## Introduction

Current common treatment for early-stage prostate carcinoma includes radical prostatectomy, external beam radiation therapy, temporary and permanent brachytherapy, active surveillance, and watchful waiting (1, 2).

Prostate brachytherapy treatment has been reported to produce excellent 10- and 15-year oncologic outcomes with relatively low morbidity (3−9). Transrectal and transperineal ultrasound approaches have evolved since their introduction in clinical practice, combining implant philosophy (preplanning, intraoperative-, and brachytherapy planning with inverse treatment planning), loading techniques (linked seeds, loose seeds), and also manual and automatic seed delivery.

These advances help increase the quality of implant which has been associated with improved biochemical recurrence-free survival (bRFS) (10, 11). The aim of this study was to report our single-institution experience on

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a homogeneous population of patients treated with brachytherapy and automated isotope delivery vs. manual loading.

## Methods and materials

The American Brachytherapy Society, European Society for Radiotherapy and Oncology, and European Association of Urology recommend brachytherapy for patients with T1-T2a, Gleason 6, and prostate-specific antigen (PSA) <10 ng/mL (12, 13). All patients referred to Institut Bergonié for brachytherapy from June 2002 to December 2010 were considered. Patients underwent a pretreatment evaluation of the medical history, physical evaluation, and prostate magnetic resonance imaging. The eligibility criteria were stage T1c T2ab N0 M0, Gleason 6 (3 + 3) or (3 + 4), baseline PSA <15 ng/mL, and prostate volume ≤50 $cm^3$.

### *Statistical methods*

The statistical analysis was performed using the SAS 9.3 software. Here, we have used classical method for the description of study population: frequencies and percentages were reported for the categorical variables; mean, median, minimum, and maximum were reported for the continuous variables.

For exploratory analyses, comparisons were performed (e.g., between strata) for continuous variables, using the nonparametric Wilcoxon two-sample test, and the Wilcoxon signed-rank test for paired data (e.g., between different points in time). For categorical variables, $\chi^2$ test or Fisher's exact test was used. Statistical significance was achieved at a $p$-value of <0.05.

Median follow-up was calculated using the reverse Kaplan−Meier method and reported with its 95% confidence interval. bRFS was calculated using the Kaplan−Meier method and reported with its 95% confidence interval. bRFS was calculated from the date of start brachytherapy to the date of biochemical recurrence or date of death whatever its cause, or the date of the most recent follow-up (censored data) (14). Log-rank test was used to evaluate differences in survival curves.

We performed a regression by the Cox model. Univariate analysis devoted to the bRFS was performed according to technical (manual/automated), clinical, pathologic (low risk/intermediate risk), and dosimetric parameters ($V_{144}$ Gy prostate [percentage of prostate receiving the prescribed dose] ≥90%, $D_{90}$ prostate [dose received by 90% of the prostate] >140 Gy), PSA bounce, PSA nadir, and use of androgen deprivation therapy.

We used a step-by-step backward selection from all significant variables at 10% threshold in univariate analysis. Only the variables significant at 5% threshold were retained in the model. The hypothesis of proportionality of risks was tested by the residue method.

### *Treatment*

For all patients, a multidisciplinary team meeting validated the treatment strategy. Brachytherapy was performed under general anesthesia. Two implantation techniques were used in our study. From June 2002 to April 2005, the implantation was based on Batterman's technique involving manual loading of Rapid Strand Oncura (IMC6611).

We used a bimodal ultrasound probe mounted on a stepper, driven by a proprietary electronic mover controlled by a computer (Spot Pro). After positioning the Foley catheter, the ultrasound probe was placed in the patient to acquire prostate images. The probe could be rotated along its axis for longitudinal acquisition through the Biprost software. An automated three-dimensional reconstruction of the prostate volume that provides axial, sagittal, and coronal planes of the acquired volumes was obtained.

Prostate, urethra, and rectum were contoured on these images by the physician. The treatment plan was manually generated by the physicist (placement of the needles and the seeds in the Spot software developed by Nucletron BV based on dose criteria constraints that have been fulfilled).

A 144 Gy dose was prescribed to the clinical target volume that encompassed the prostate (clinical target volume) based on European Society for Radiotherapy and Oncology, European Association of Urology, and European Organization for Research and Treatment of Cancer recommendations (15).

Once the dosimetric criteria were validated by the radiation oncologist, needles were inserted, one after another, and under ultrasound guidance on the longitudinal view. The software helps guiding the needle insertion by providing an outline of the planned needle location overlaid on the live ultrasound image.

Subsequently, according to the dosimetry planning, the manual loading was carried out with seeds Strand in vicryl suture—Rapid strand Oncura (IMC6611)—with 0.45 μGy/h at 1m activity per seed followed by retraction of each needle.

Each patient had a pelvic CT at Day 1, and dosimetry was performed, following which the urethra catheter was removed and patient was allowed to leave the hospital with a prescription for α-blockers and anti-inflammatory medication, if possible. A pelvic CT scan was performed to check the dosimetry 1 month after brachytherapy.

Since May 2005, we switched to automated seed implantation, the Nucletron First system. This system is a remote afterloader, the seed Selectron, connected to the Spot TPS treatment planning system, and the electronic mover of the ultrasound probe allows seed spacer train delivery according to the planning information. The activity of each seed was automatically checked. The train (active selected seeds and inactive seed spacer) is delivered by the remote after-loader seed Selectron and retracts the