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CLINICAL INVESTIGATION **Prostate**

BYPASSING THE LEARNING CURVE IN PERMANENT SEED IMPLANTS USING STATE-OF-THE-ART TECHNOLOGY

Luc Beaulieu, Ph.D.,* Dee-Ann Radford Evans, M.Sc.,† Sylviane Aubin, M.Sc.,* Steven Angyalfi, M.D.,† Siraj Husain, M.D.,† Ian Kay, Ph.D.,† André-Guy Martin, M.D., M.Sc.,* Nicolas Varfalvy, M.Sc.,* Éric Vigneault, M.D., M.Sc.,* and Peter Dunscombe, Ph.D.†

*Département de Radio-oncologie, Centre Hospitalier Universitaire de Québec, Hôtel-Dieu de Québec, Québec, PQ, Canada; †Departments of Radiation Oncology and Medical Physics, Tom Baker Cancer Centre, Calgary, AB, Canada

Purpose: The aim of this study was to demonstrate, based on clinical postplan dose distributions, that technology can be used efficiently to eliminate the learning curve associated with permanent seed implant planning and delivery.
Methods and Materials: Dose distributions evaluated 30 days after the implant of the initial 22 consecutive patients treated with permanent seed implants at two institutions were studied. Institution 1 (I1) consisted of a new team, whereas institution 2 (I2) had performed more than 740 preplanned implantations over a 9-year period before the study. Both teams had adopted similar integrated systems based on three-dimensional (3D) transrectal ultrasonography, intraoperative dosimetry, and an automated seed delivery and needle retraction system (FIRST, Nucletron). Procedure time and dose volume histogram parameters such as D90, V100, V150, V200, and others were collected in the operating room and at 30 days postplan.
Results: The average target coverage from the intraoperative plan (V100) was 99.4% for I1 and 99.9% for I2. D90, V150, and V200 were 191.4 Gy (196.3 Gy), 75.3% (73.0%), and 37.5% (34.1%) for I1 (I2) respectively. None of these parameters shows a significant difference between institutions. The postplan D90 was 151.2 Gy for I1 and 167.3 Gy for I2, well above the 140 Gy from the Stock *et al.* analysis, taking into account differences at planning, results in a p value of 0.0676. The procedure time required on average 174.4 min for I1 and 89 min for I2. The time was found to decrease with the increasing number of patients.
Conclusion: State-of-the-art technology enables a new brachytherapy team to obtain excellent postplan dose distributions, similar to those achieved by an experienced team with proven long-term clinical results. The cost for bypassing the usual dosimetry learning curve is time, with increasing team experience resulting in shorter treatment times. **© 2007 Elsevier Inc.**

Prostate brachytherapy, Dosimetry, Inverse planning, Seed activity, Seed misplacement, Seed migration, Computer optimization, Automated delivery, Intraoperative.

INTRODUCTION

In almost all prostate brachytherapy programs, it is seen that the quality of the implants, as measured by postplanning dosimetric indices (1), increases with the number of procedures performed up to about 70 to 100 procedures. This effect is known as the procedure learning curve. It is also known that outcome in terms of tumor control probability has been linked to the dose distribution, in particular the dose received by 90% of the prostate volume, or D90 (2, 3), and that V100 could also be a good clinical indicator of success (4). In a multi-institutional study, Bice *et al.* showed that the prostate volume receiving 100% of the prescribed dose, or V100, correlates with the number of procedures (5). In another study, Lee *et al.* analyzed the dose distributions of their first group of 30 patients compared with a subsequent group of 33 patients (6). These investigators found that V100 increased from 75.8% to 85.2% ($p = 0.0006$), and that for their last 10 patients V100 was 88.7%. All of

Reprint requests to: Luc Beaulieu, Ph.D., Département de Radio-oncologie, CHUQ-HDQ, 11 Cote du Palais, Québec, PQ, G1R 2J6, Canada. Tel: (418) 525-4444, ext. 15315; Fax: (418) 691-5268; E-mail: beaulieu@phy.ulaval.ca

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Table 1. Technology and logistical differences between the two treatment centers

	I1	I2
Patients receiving implants before implementation of FIRST system	0 patients	740 patients
Source strength	0.52 U (0.4mCi)	0.76 (0.6mCi)
Planning system	SPOT vs 2×	SPOT vs 3×
Intraoperative planning	Manual, interactive	Inverse, interactive
Contouring tools	Single view	Multiview
Planning technique	Intraoperative, manual	Intraoperative, inverse
Intraoperative delivery	seedSelectron afterloader	seedSelectron afterloader

Abbreviations: I1 = Institution 1 (Tom Baker Cancer Centre); I2 = Institution 2 (Centre Hospitalier Universitaire de Québec).

the above studies were based on pretreatment planning and manual needle loading.

Since the introduction of prostate brachytherapy in the early 1980s, many technologic advances have taken place that make the implantation procedure more precise: inverse-planning optimization engines for optimal seed placement (7, 8), three-dimensional ultrasound (3D US) technology (9, 10) with real-time needle guidance (10), real-time seed detection on fluoroscopy (11–14), and the recent availability of flat-panel cone-beam tomography units are some examples (15–17). Parallel to the evolution of the technology, intraoperative procedures were developed and compared with conventional pretreatment planning (18–20). For all cases, intraoperative planning results in better postimplantation target coverage and protection of the organs at risk. Intraoperative preplanning is now recommended by the American Brachytherapy Society (21).

This article examines the clinical impact of using state-of-the-art technologies in a new prostate brachytherapy program. In particular it addresses the question: does the clinical adoption of these technologies contribute to more accurate seed delivery and better implant quality, especially for new centers? This study looks at the first permanent seed implants performed using similar equipment at a center new to prostate brachytherapy and those implanted by a center experienced with preplanned manual implants. The end point of the study is the 30-day postplan dosimetry.

METHODS AND MATERIALS

The first 22 consecutive patients treated with iodine-125 seed implants, using the FIRST™ system (Nucletron B.V., Veenendaal, The Netherlands) for localized low risk cancer at two Canadian institutions are included in the analysis. Institution 1 (I1), The Tom Baker Cancer Centre, started their prostate implant program and treated their first patient in 2003. The patients included in this study are the first 22 patients in the program. The Tom Baker Cancer Centre has now performed over 200 implants. Institution 2 (I2), Centre Hospitalier Universitaire de Québec (CHUQ), has had an ongoing seed implant program since 1994 (first Canadian program). Before adopting the FIRST system in 2004, CHUQ had performed 740 implantations using a preloaded needle technique (loose seeds). At the start of this study, the outcomes in the first 480 patients at CHUQ was 93.5% at 5 years (median follow-up, 42 months; maximum, 113 months), with an excellent toxicity profile (22, 23).

Patients treated at both centers had favorable prognoses. Eligible patients met the following criteria: stage T1 to T2b disease, prostate-specific antigen (PSA) <10, a Gleason score ≤ 6, and a prostate volume <50 cc. A follow-up at 4 weeks was scheduled at which a CT scan, or postimplantation dosimetric evaluation based on the American Brachytherapy Guideline (1) and X-ray films (number of seeds and migration to lung, I2 only) were taken. American Urological Association prostate symptom score (AUA score) (24), sexual function, APS level, and other toxicity and quality-of-life parameters were acquired before the procedure and at follow-up at 3 months, 6 months, 12 months, and once every year afterward.

At both centers, a biplanar transrectal US probe is used to acquire images for planning in the operating room (OR). The probe is mounted on a calibrated stepper and attached to an electronic mover. The electronic mover is controlled by the computer planning system. The planning system captures the live feed from the US unit as the mover rotates the probe capturing sagittal slices of the prostate at 0.5° or 1° intervals for up to 140° of rotation. The probe position is calibrated against the delivery template. The image is reconstructed in three-dimensional (3D) form in the planning system, and a complete 3D data set containing the prostate and all the organs at risk can be used for planning purposes. A Foley catheter is used and allows localization of the urethra in the reconstructed image (neither gel nor contrast agent is necessary). Reconstructed transverse images at 2.5-mm or 5-mm increments are used for contouring. The base and the apex can also be seen in the sagittal and coronal planes. In the OR, only the prostate and the urethra were contoured for this study. A plan is then generated on the contoured structures (the planning method will be discussed later here).

In the FIRST system, the needle navigator tool and electronic mover allow the user to control the rotation of the US probe with respect to the template defined coordinate system. At the time of needle insertion, the sagittal transducer of the US probe is set in the longitudinal plane of the needle to be inserted. A virtual needle track is presented to the physician as a guide to where the needle should go. If the needle is not inserted perfectly in the virtual track, it can be corrected interactively on the planning system. This feature was not available in the software release available to I1. For their first 22 patients, I1 needles were implanted using transverse views of the prostate at the appropriate needle depth. Planning adjustments such as seed-loading updates and needle-position changes were done interactively but manually in the system as required.

In the I1 and I2 procedures, all of the needles were inserted