# *Options and recent advances in permanent brachytherapy for prostate cancer*

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*Permanent interstitial brachytherapy with I-125 or Pd-103 seeds is a well-established approach as single modality for low-risk prostate cancer patients and as part of a multi-modality program for intermediate- and high-risk patients. There are multiple approaches that have been developed to deliver high-quality implants, including pre-planned and real-time intra-operative techniques. In the hands of experienced users, either approach can provide consistently excellent outcomes. We believe that the combination of real-time intra-operative dosimetry and connected seeds may provide for improved consistency due to decreased seed migration.*

**Key Words:** prostate cancer, brachytherapy, dosimetry, loose seeds, linked seeds

## Introduction

Brachytherapy using permanent interstitial placement of I-125 or Pd-103 seeds has become an established treatment modality for prostate cancer. Effective as a single modality for low-risk patients,[1-3] it has also been shown to be effective for intermediate- and high-risk patients when combined with hormonal therapy and external beam radiotherapy.[2,4,5] Long-term data with around 6 years median follow-up reveals actuarial PSA-relapse free survival rates of 91%-88% for low-risk patients at 8-12 years.[1-3] For higher risk patients, Potters et al report actuarial rates of PSA-relapse free survival of 80% for intermediate-risk patients and 66% for high-risk patients, with a mean follow-up of 82 months.[2] Kupelian and colleagues report actuarial PSA-relapse free survival of approximately 75% at 7 years with a median follow-up of 46 months.[4] Stock et al, at Mount Sinai School of Medicine (MSSM), with a median follow-up of 50 months, reports actuarial PSA-relapse free survival of 86% at 5 years for high-risk patients[5] with a combination of 9 months of hormonal therapy, brachytherapy, and external beam radiotherapy.

The importance of implant dosimetry in regards to tumor control is well recognized. One dosimetric factor that has been consistently associated with tumor control is the D90; that is, the minimum dose to 90% of the prostate. A D90 at or above 140 Gy for I-125 implants[6] or 90% of the prescription dose[2] have been shown to correlate with biochemical control. There are multiple techniques that provide for designing and implementing effective seed implants with appropriate dosimetry.[7] Two basic approaches are pre-planning and real-time intra-operative planning.

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## Pre-planning approaches

The patient usually has an ultrasound study done before the date of the implant and a plan for seed placement is developed and refined based on that study. Then, once in the operating room (OR), the position that the patient was in during the planning study is reproduced as closely as possible. The seeds are then placed according to the plan developed earlier. Seeds are placed in the prostate using pre-loaded needles or strands of connected seeds prepared earlier according to the pre-plan. Some pre-planners also use gun-type applicators of loose seeds, such as the Mick applicator (Mick Radio-Nuclear Instruments, Mount Vernon, New York, USA). Minor modifications can be made if there is difficulty reproducing the pre-plan.

## Real-time intra-operative planning

No pre-procedure imaging study is used to develop a plan, although some form of volume study is used to determine how many seeds to order. The patient is taken to the OR and positioned to avoid pubic arch obstruction, and the plan for seed placement is developed in the OR based on the shape and position of the prostate at that moment. Real-time intra-operative dosimetry for permanent seed brachytherapy for prostate cancer has multiple advantages over pre-planning techniques, as well as some disadvantages. Real-time intra-operative planning allows for optimization during the procedure by visualizing seed deposition and the resulting isodose lines. This allows for optimization of the plan to account for changes in prostate size and shape with needle placement, needle deviation from planned position, and for seed movement after seed deposition. Disadvantages include typically longer OR times with real-time dosimetry and, commonly, use of the Mick applicator to place loose seeds, which some users find unwieldy. Advantages of the Mick applicator include the ability to place individual seeds precisely and a great deal of flexibility on seed arrangement. However, seeds can move from their original location, or migrate, a small distance or farther, even to the lungs or other remote locations.[8-10] Loose seeds seem to migrate more frequently then connected seeds, especially when seeds are placed outside the prostate.[11,12] Connected seeds have been found to improve implant dosimetry by some investigators[13] while other investigators have found no difference, at least when implanted inside the prostate.[14]

## Hybrid approaches

In an attempt to combine the advantages of real-time intra-operative dosimetry and connected seeds, we have developed a method of constructing custom-made links of seeds in the OR. Computed tomography volume studies are performed 2 weeks before the date of the brachytherapy procedure. The volume of the prostate is used to determine the activity of seeds to order based on the MSSM nomograms. Patients are then taken to the OR and the general technique developed by Stock and Stone at MSSM[15] is implemented using the Variseed brachytherapy planning system (Varian Medical Systems, Palo Alto, California, USA). An initial intra-operative plan is then developed using the ProSeed™ planning module (C.R. Bard, Inc., Covington, Georgia, USA) within VariSeed. Needles are placed in the periphery of the gland approximately 1 cm apart. The plan is then re-optimized for the actual location of the placed needles. Longitudinal views of the prostate are used to measure the length of the prostate for an individual needle path. A push-button delivery system, the QuickLink device (C.R. Bard, Inc., Covington, Georgia, USA), is then used to construct links of the appropriate number of seeds for the length measured on the longitudinal view on the ultrasound, according to the real-time intra-operative plan, Figure 1. The linked seeds are then transferred to the appropriate needle already placed in the patient via a hand-held transfer device. The linked seeds are then deposited as a single unit into the prostate under ultrasound visualization on the longitudinal view, in a manner analogous to that used with a pre-loaded needle. The needle is removed as the linked seeds are placed. The process is repeated until all the peripheral needles have been used to place the peripheral seeds. Approximately 75% of the required

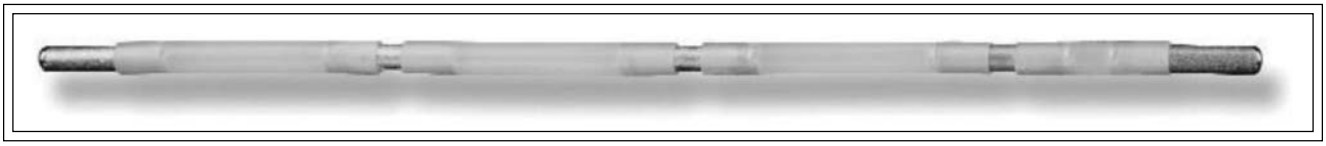

**Figure 1.** An example of a five-seed custom-designed link of connected seeds made with the QuickLink device (C.R. Bard, Inc., Covington, Georgia, USA) push-button delivery system. Note the non-uniform seed distribution.

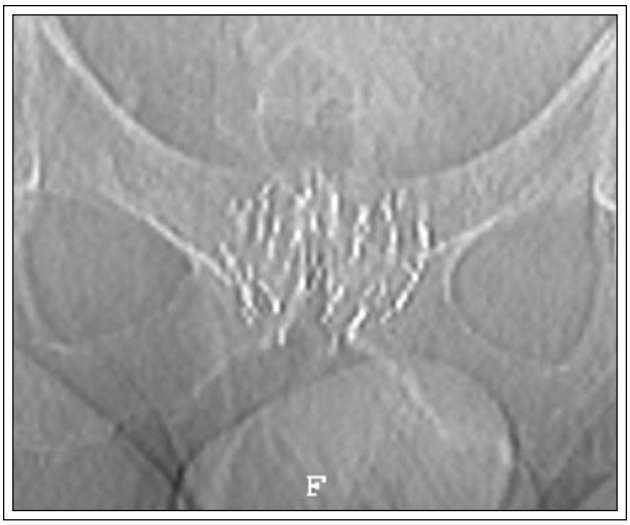


**Figure 2.** A computed tomography scout image of an I-125 seed implant using custom-made links of connected seeds using the QuickLink device (C.R. Bard, Inc., Covington, Georgia, USA) push-button delivery system.

activity is placed in the periphery of the gland. Next, the process is repeated for inner needles, typically 5-7, in order to place the remainder of the required activity. Most of this is implanted in the base and apex of the gland, to "cap" the prostate. The dosimetry is optimized once again to determine the optimal seed locations based on the actual location of the inner needles. Once the final plan is approved, the inner seeds are placed in the same manner as those of the peripheral needles, using custom-built links of connected seeds using the QuickLink device push-button delivery system, according to the length of the needle path in the prostate and the final intra-operative plan.

To date, 20 patients at our institution have had real-time intra-operatively planned implants with linked seeds using the QuickLink device and at least 1 month of follow-up with post-implant CT scans for dosimetry. Figure 2 displays a scout view from a post-implant CT scan of a patient treated with this approach. Fifteen patients had I-125 implants prescribed to a D90 of 160 Gy and five patients had Pd-103 implants prescribed to a D90 of 100 Gy followed by external beam radiotherapy. Post-implant CT dosimetry revealed a median D90 of 166.4 Gy (range 142.5-184.8) for the I-125 implants and 93.2 Gy (range 88.8-119.4) for the Pd-103 implants. Rectum and urethra doses were also within acceptable ranges. Only one patient required temporary urinary catheterization (crude rate of 5%). Intra-operatively planned permanent brachytherapy using real-time techniques with custom constructed linked seeds made intra-operatively with the QuickLink device is feasible and preliminary dosimetric results are encouraging. We believe this approach provides an excellent combination of the flexibility of real-time intra-operative planning with the decreased seed migration of connected seeds, and continue to refine this method at our institution.

## Disclosure

Dr. Marshall is consultant for C.R. Bard, Inc.

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