

Low Dose Rate Brachytherapy in Prostate Cancer

Dr Cattleya Gaspar

"Oncology is a remarkable field. With advances in medical sciences and technology, there are continuous opportunities on the horizon to improve patient care and treatment outcomes. I remain grateful for the mentorship by some of the greatest minds in the field, and have dedicated my career to help those impacted by cancer" - Dr Cattleya Gaspar.

Dr Gaspar completed her MBChB at the University of Pretoria in 2011. Having served two years of medical internship at the Steve Biko Academic Hospital, in Pretoria, Dr Gaspar then completed her community service at the Kalafong Tertiary Hospital in family and emergency medicine. She then returned to the Steve Biko Academic Hospital in 2015 where she worked as a medical officer in Medical Oncology. After eighteen months, Dr Gaspar started her specialisation and was admitted as a Fellow of the College of Radiation Oncologists in 2021. She joined De Mûelenaere Oncology (DMO) in 2022, where she is now a director.

Dr Gaspar has completed her Master's Degree at the University of Pretoria, with her research focused on the predisposing factors of chronic radiation proctitis. She enjoys academics and attends both local and international meetings, to continuously broaden her expertise - she recently attended the ESTRO-EAU Multidisciplinary Management of Prostate Cancer Course as well as the ESTRO Brachytherapy for Prostate Cancer course in Verona, Italy. Dr Gaspar is currently receiving training at the De Mûelenaere Oncology practice, to perfect her LDR brachytherapy skillset.

Dr Gaspar works at the Groenkloof Radiation Oncology and Mûelmed Aracdia Radiation Oncology Centres and is part of a team of Oncologists that consult at the DMO locations. Her areas of interest include genito-urinary cancers.



Introduction

As most of us are aware, prostate cancer is one of the most common cancers in men, with a wide variation in incidence and mortality worldwide. The management of a patient diagnosed with prostate cancer usually includes several modalities. Characteristics such as the stage of the cancer, the patient's risk category, the cancer biology and of course the patient's overall clinical condition (performance status, co-morbidities and life expectancy at diagnosis) would guide the treating specialist on selecting the most appropriate management plan.

Low Dose Rate (LDR) Brachytherapy in the management of prostate cancer has been around since the 1970s, with the introduction of Iodine-125 and Palladium 103 seed implants. It is a well-established curative option for appropriately selected patients. It has been evaluated in multiple randomised and prospective trials.

Low dose rate (LDR) refers to the delivery of radiation at a slow, continuous rate. In prostate brachytherapy, it specifically means delivering radiation at a rate of 0.4-2.0 Gy/h^[1] by using radioactive seeds.

The radio-active seeds are permanently implanted within the prostate gland and with the process of radioactive decay, these seeds release local radiation within the prostate gland tissue. This allows for DNA damage of the malignant cells, while allowing the healthy tissues to repair. Eighty percent of the dose delivered by LDR brachytherapy occurs within the first two months after insertion.

Advantages of LDR brachytherapy:

- Superior form of conformal radiotherapy – tightest achievable dose distribution and allows for dose escalation far beyond what is safe with external beam radiotherapy alone (i.e.) high precision and efficacy

- Convenient and fast patient recovery, with minimal side effects compared to other treatment options. The procedure is typically performed as a one-time, same-day surgical, outpatient procedure, causing minimal disruption to daily life.
- Cost effective with excellent long term proven results – in the correctly selected patient, progression free survival can be > 90% at 10 to 15 years ^[2].

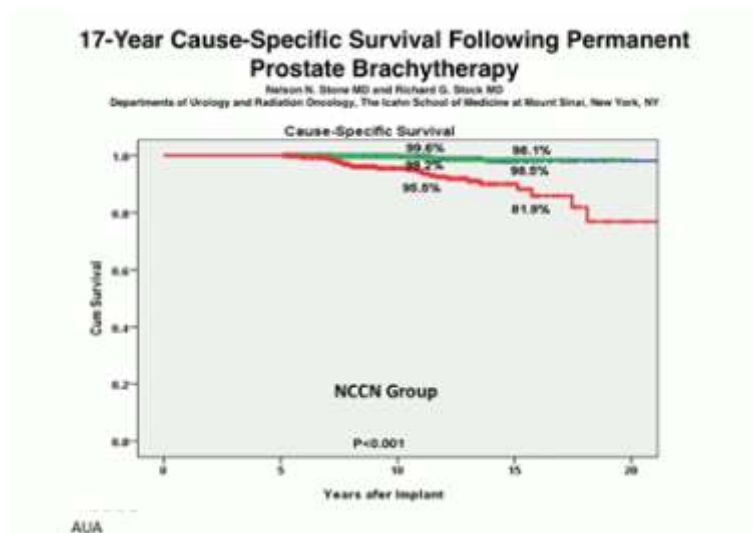
LDR Brachytherapy: Monotherapy

Patient selection

Brachytherapy is mainly indicated for *localised prostate cancer*. Patient selection is based on tumour risk, urinary function and prostate anatomy.

According to the 2012 ABS guidelines ^[3], patients who benefit most from LDR brachytherapy are those with a PSA (ng/ml) <10, a Gleason score of 5-6, a stage T1c-T2a, an IPSS of 0-8, a prostate volume of <40 g and a Qmax of >15 ml/s.

Patients who do poorly with LDR brachytherapy are those with a PSA (ng/ml) >20, a Gleason score of 8-10, T3 disease, an IPSS >20, a prostate volume of >60 g and a Qmax of <10 ml/s.



Stock & Stone (J Urol 2014) publication

In other words, patients with *NCCN low risk disease* with a relatively good bladder function and minimal LUTS benefit the most from LDR monotherapy.

We also see this finding in the Stock & Stone (J Urol 2014) publication ^[2], which showed that in 1,669 men with localized prostate cancer, treated with LDR brachytherapy (+/- ADT +/- EBRT), there was a 15 year cancer specific survival (CSS) of 96 % in patients with NCCN low risk disease.

Similarly, there was a 15 year CSS of >90% in patients with intermediate risk disease. This poses the question: how does one manage the intermediate risk group? Are those patients suitable for LDR brachytherapy as monotherapy?

Several studies have shown that LDR brachytherapy as monotherapy is suitable for the patients with intermediate risk disease, but in the *favourable* intermediate risk category.

The RTOG 0232 phase III randomised trial ^[4] compared LDR brachytherapy alone vs LDR brachytherapy + external beam radiotherapy in intermediate risk disease. There was no improvement in progression free survival with combined therapies in the *favourable* intermediate risk groups. Combination treatment caused increased toxicity.

How does the age of the patient influence patient selection?

In younger men (<50- 60 years old), with localised prostate cancer, both radical prostatectomy and LDR brachytherapy provide favourable long-term results. Randomised evidence shows comparable prostate cancer-specific survival among definitive treatments, with differences primarily in toxicity profiles, rather than mortality ^{[5] [6]}. In younger patients, life expectancy may exceed 20 years, therefore, treatment choice should weight durability of control versus functional outcomes.

Surgery is often favoured in young, healthy men due to longer life expectancy and salvage flexibility/salvage options (i.e.) there are more established treatment options after disease recurrence following a radical prostatectomy. However, LDR brachytherapy, supported by randomised data, in selected risk groups, still remains an effective alternative.

Albeit a challenging topic to discuss, the takeaway message is that each patient's case should be individualised, carefully reviewed and discussed in a MDT forum. This will ensure

the best treatment outcome for the patient.

LDR Brachytherapy Contra-indications ^[1]

- Medically unfit to have general or spinal anaesthesia.
- Life expectancy of <5 years / widespread metastases
- Prostate size >50 g (risk of pubic bone interference)
- Recent or unhealed TURP (within 3-6 months)
- Bleeding disorder
- Previous pelvic radiation
- IPSS >20
- Large median lobe (risk of urinary retention)
- Rectal fistula

LDR Brachytherapy Procedure and Planning

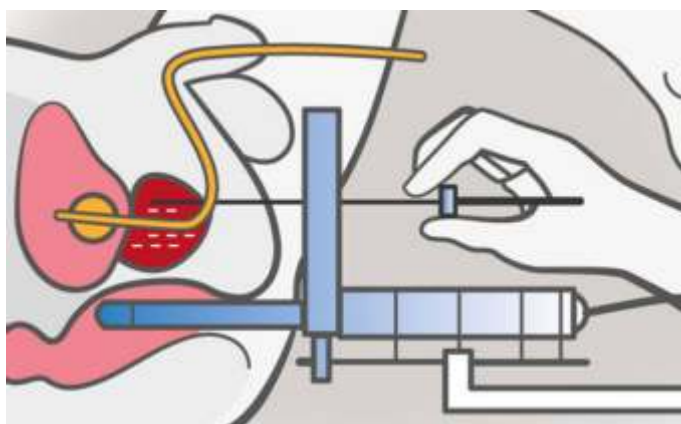
The patient is usually admitted the day of the procedure. Pre-op bowel preparation is necessary, and spinal, epidural, or general anaesthesia is generally used. A urinary catheter is then inserted. A trans rectal ultrasound (TRUS) is used to locate the prostate, urethra and seminal vesicles. The TRUS is supported on an adjustable 0.5 cm stepping unit mounted to the operating table. Images of the relative structures are obtained, delineated and the treatment template is planned.

Needles are then inserted through the template holes until they are viewed in the desired plane. The radioactive seeds are deposited from preloaded needles or the

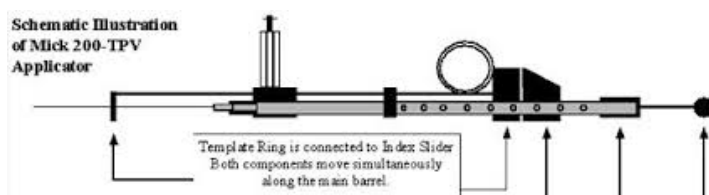
"Mick applicator". Each seed is placed in the appropriate position, being aware of the dosimetric parameters that need to be met.

The goal of treatment planning is to cover the prostate with a 3–5 mm margin (for potential extra capsular extension) ^[1] Brachytherapy monotherapy doses range between 144 and 145 Gy to 100% isodose with a V100 CTV > 95% ^[7].

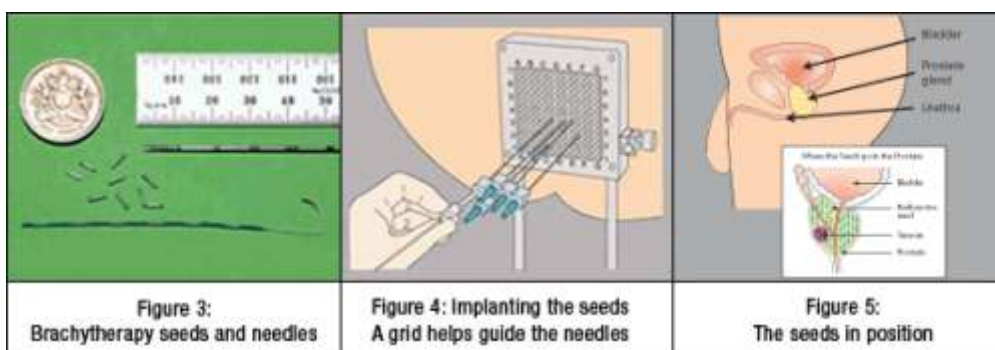
Typically, after the procedure, the patient is discharged once he is able to urinate and seed placement has been confirmed on imaging. The patient is discharged on stool softeners, antibiotics and anti-inflammatories and then followed up by the urologist and oncologist accordingly.



^[8] The seeds are placed precisely with the help of high-resolution ultrasound, which provides a three-dimensional image of the prostate and neighbouring organs (rectum and bladder).



^[9] The radioactive seeds are deposited from preloaded needles or the "Mick applicator".



^[10] Figure 3 (above) shows the size of the seeds and needles used. Figure 4 (above) shows an illustration of how the needles are guided using a grid for precision and accuracy.

LDR brachytherapy side effects ^[1]:

Generally, treatment is well tolerated with minor post procedure side effects. Peri-operative complications may include pain, dysuria, haematuria, urinary frequency or retention. Obstructive symptoms occur in <1–10 % of men and tend to resolve six to twelve months after the implant. Urethral strictures, severe rectal bleeding, rectal fistulas and erectile dysfunction are very rare complications.

LDR brachytherapy: Combination treatment?

The ASCENDE-RT randomised phase III trial ^[11] compared external beam radiotherapy alone vs external beam radiotherapy plus a LDR brachytherapy boost. The brachytherapy boost significantly improved biochemical control in the *unfavourable* intermediate risk and *high-risk* patient groups. Although there were higher rates of genitourinary toxicity in the LDR brachytherapy boost arm, a brachytherapy boost demonstrated the potency of dose escalation in higher risk disease.

Conclusion

LDR brachytherapy is an effective, minimally invasive, and established standard of care for localized prostate cancer, offering long-term biochemical control comparable to other modalities such as radical prostatectomy and external beam radiation therapy, particularly for *low to favourable intermediate-risk* patients. It is a cost-effective modality and treatment is usually well tolerated with minimal treatment related side effects.

Prostate cancer has become one of the most common malignancies world-wide. Many patients are diagnosed with early-stage disease. Management options vary, however, each patient's case should be individualised and discussed at a MDT forum. This will ensure the best treatment outcome for the patient.

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